Kenneth D Gardner.

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SURGICAL PATHOLOGY

AND

THERAPEUTICS

BY

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FELIX QVI POTVIT RERVM COGNOSCERE CAVSAS
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PREFACE.

THE scientific portion of a surgical education was formerly regarded as something apart and ornamental, but it has now become an eminently practical feature of the student's curriculum.

No young practitioner can be regarded as thoroughly equipped for surgical work who is not both a good pathologist and an expert bacteriologist. The confidence born of a knowledge of Pathology and Bacteriology enables him to assume grave responsibilities and to grapple successfully with the most complicated problems. It is from men thus equipped that we have a right to hope that the future masters of surgery are to be evolved.

An attempt is therefore made in this book to associate pathological conditions as closely as possible with the symptoms and treatment of surgical diseases, and to impress upon the student the value of these lines of study as a firm foundation for good clinical work.

It is the Author's hope that the following pages will present to a large number of practising physicians, in a readable form, many subjects that received but little attention when they graduated.

The illustrations by Mr. William J. Kaula are, with one or two exceptions, original. The drawings of microscopical sections are taken from specimens prepared for the purpose, and are intended to illustrate as closely as possible the results of modern microscopical technique.

The Author takes this opportunity to acknowledge his indebtedness to Dr. Arthur K. Stone for valuable assistance, and to express his appreciation of the courtesy extended to him by many of his colleagues during his labors.

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SURGICAL PATHOLOGY AND THERAPEUTICS.

I. BACTERIOLOGY.

IF one were to search literature for the earliest accounts of the germ-theory of disease, it might be necessary to consult the oldest writings of which we have any knowledge, for even among the ancients there were those who thought that disease was due to the invasion of the system by minute organisms. But it remained for Leeuwenhoek, in 1675, actually to demonstrate with his rude microscope the presence of infusoria in the saliva. The theory of a *contagium vivum* was taken up from time to time after that date, and Robert Boyle, a prominent writer of the same century, maintained that he who obtained a proper comprehension of fermentation would be able to interpret satisfactorily the various phenomena of disease, particularly of fevers. Spallanzani, in the eighteenth century, and after him Gay-Lussac, in 1810, experimented with fermentation. Cagniard-Latour and Schwann, in 1837, recognized that alcoholic fermentation was due to the presence of a living organism, the yeast plant; but this view was opposed with all the weight which the authority of Liebig could bring to bear upon it, who believed that fermentation was of a purely chemical origin.

In 1840, Dr. Farr applied the term "zymotic" (ζύμωσις, a ferment) to certain diseases supposed to be due to a fermentative process. Ten years later Davaine demonstrated the bacillus anthracis in the bodies of animals which had died of splenic fever. It was at that time thought, however, that disease might arise *de novo*, and that, although organisms might be present, it was possible that they might have been formed by "spontaneous generation." It was not, however, until Pasteur, in 1858, unveiled the mysteries of fermentation, and later disproved the theory of spontaneous generation, that the relation of micro-organisms to disease began to be understood. Pasteur's law of fermentation has been likened in its importance to Newton's law of gravitation. It is undoubtedly to him that credit should be given for furnishing the first reliable data from which the modern science of bacteriology has been evolved. Davaine, stimulated by Pasteur's researches, renewed his studies of the bacillus of anthrax, and fully identified the organism as the cause of the disease. This bacillus may therefore be placed, chronologically, at the head of the list of pathogenic bacteria.

Pasteur showed also that putrescence is a form of fermentation due to the presence of micro-organisms, and he demonstrated that the changes taking place in the secretions of a wound were of a similar character. It was at about this time (1865) that Lister began to appreciate the bearing of this scientific work upon surgery, and commenced his studies upon the antiseptic treatment of wounds. This gave a powerful impetus to the study of the relation of micro-organisms to disease. No great advances were made at first, and much of the work done by Pasteur and his pupils at that period in the study of the diseases of man suffered for the want of suitable methods of investigation. Bacteria were cultivated almost exclusively in liquids, the bouillon of Pasteur. The cut surface of potatoes was found to give an idea of the coarse appearance of the growths, which the bouillon failed to show. When, finally, solid media were substituted as soil for the growths of the organisms—an improvement for which we are indebted to Koch, the great German observer—the separation of bacteria, and consequently their identification, for the first time became possible.

Bacteria belong to the lowest order of the vegetable kingdom, and, with a few apparent exceptions, they may be said to form one group of the fungi, the schizomycetes or fission-fungi, in distinction from saccharomycetes or yeast-fungi, which produce alcoholic fermentation, and the mucorini or mould-fungi. The fungi are chiefly distinguished by the absence of chlorophyll, and therefore by their lack of power to assimilate inorganic substances, being thus dependent for their food upon living or upon dead organic matter obtained from other plants or from animals. Bacteria derive their name from βακτήριον, a rod, which many of them resemble in shape.

The developed organism is in form a cell with a membrane and contents, but no nucleus. The contents consist of a more or less homogeneous protoplasm. This protoplasm possesses, in common with the nuclei of the cells of the tissues of the body, the property of being strongly stained by the aniline dyes. It is surrounded by a delicate membrane, which, according to Thoinot, appears like a condensation of the peripheral layers of the protoplasm, from which it is with difficulty separated. According to De Bary, this membrane is a condensation of the innermost and most compact layers of a gelatinous envelope, and consists of a substance closely allied to cellulose. When stained with aniline dyes the difference between protoplasm and envelope is not visible, but by special methods of treatment the contents may shrink, and the envelope then becomes more apparent; or, when treated with water, the outer layers swell up and their gelatinous nature becomes evident. The cells thus appear to be enclosed in a capsule. During the process of division this material holds the organisms together, and forms at times a zooglœa, or glue-like mass, in which they are imbedded. It is this material which may give the cultures their form and consistency when growing on solid or in fluid media. In water it collects at times in large masses after the enclosed bacteria have attained their growth and have died, and becomes an efficient aid in the sand filtration of water-supplies. Many of the bacterial growths are in the presence of oxygen highly colored, being red, yellow, green, or blue. According to some this coloring matter is in the protoplasm, but according to others it lies outside the cells, as in the case of the bacillus prodigiosus, a beautiful red growth, where the pigment is in granules which have been exuded.

A considerable number of the bacteria possess *no movement* whatever. Among these are the entire family of micrococci and some bacilli, as the anthrax and tubercle bacilli. The great majority of bacteria are, however, according to the conditions under which they live, able to change from the motile state to the non-motile, or *vice versâ*. When examined in fluid they may be seen moving about in serpentine-like curves, or they may have a sort of oscillating movement around a central axis. These movements of the bacilli are supposed by some to be effected by cilia projecting from different portions of their bodies, but these prolongations have been shown to be continuous, not with the protoplasm, but with the cell-membrane, and therefore, according to some authorities, are not organs of locomotion. Moreover, many bacilli which have active movements are found to possess no cilia whatever, being propelled by the vibratory movements of the flexible cells. The oscillations of the micrococci, so familiar to all observers, are not true movements of the cells, but are due to molecular agitation, the so-called "Brownian movement."

The principal forms of bacteria are the small globular forms, or micrococci (*κόκκος*, a berry), the bacilli or staff-shaped bacteria, and the spirilla or spiral forms. The shape of the micrococci—or "cocci," as they are often called—is usually round, although some have a more or less oval contour. There are certain prefixes to the noun coccus that indicate the different groupings which this variety of bacteria take in their growth. Thus if the cocci tend to form in pairs, or two cocci are seen still connected together, they are termed "diplococci;" those arranged in single rows of "chains" are called "streptococci;" and those grouped together in grape-like bunches are called "staphylococci." The long, staff-shaped bacteria are known as "bacilli" (*bacillus*, a rod). When unusually long they have a slightly undulating shape, and are then known as "leptothrix" (*leptothrix buccalis*). Under the head of "spirilla" are included those bacteria which take the form of an arc of a circle or of a spiral. The "comma bacilli" of cholera are included in this category. There are in bacteriological nomenclature a great variety of terms which are hardly worth studying, as some of them have been discarded altogether, and about others little will be heard in laboratory-work. The two principal forms seen in the different varieties of surgical bacteria are the micrococci and the bacilli.

Nägeli attached little importance to form: he believed that bacteria might not only change their shape from time to time, but in the course of years and under varying conditions also change in their pathogenic qualities. The same species, he believed, might at one time be concerned in the different forms of fermentation, at another in the decomposition of albuminous substances, or in typhus, cholera, or intermittent fever. The present opinion is that bacteria are divided into a limited number of varieties according to their action and form, but these varieties are never changed into other forms. The possibility of such a change from a harmless variety to a most malignant type, as Buchner supposed in the case of the hay and anthrax bacilli, is now understood to have been due to impurities of culture. Slight changes in form and appearance may be brought about by methods of preparation, staining, or culture. The organism may vary also in appearance with age and activity, but there is nevertheless a form which it always preserves as the type of its normal development.

Bacteria *multiply* either by division of the cells into two equal halves—that is, by "fission"—or by spore-formation. When a coccus divides, it becomes elongated or oval in shape, the middle portion becomes slightly contracted, and a delicate line appears between the two portions thus indicated. This line of division subsequently swells, and develops into a new membrane for each of the daughter-cells thus formed. If the mother-cell is originally separated from other cells, this division forms the so-called "diplococcus." If, on the contrary, a number of cocci are attached to one another and remain so during division in a linear direction, we have the "streptococcus" formation. If the fission takes place in two directions perpendicular to one another, we have as a result an arrangement of the cells such as is seen in the micrococcus tetragenus. If, however, segmentation takes place in different directions in the different cells, then we obtain the grouping of cells characteristic of the "staphylococcus." Each form of micrococcus develops according to one of these methods alone, and never varies in its mode of growth. The bacilli elongate slowly before fission, but the division of this form is not so easily recognized as that of the cocci.

A number of bacilli and a few spirilla, after going through different stages of development, ultimately undergo sporulation before the cell is finally destroyed. When sporulation takes place, the protoplasm seems to shrink together at certain points into denser masses, that may grow in a few hours to an oval, a round, or even a staff-like, structure, which refracts the light more strongly than the surrounding protoplasm. The spore thus formed possesses an extremely dense enveloping membrane, which, like the covering of vegetable seed, protects it from external influences until it can find conditions favorable for future growth. The cell is somewhat distended by the spore, which may occur either in the middle or at the pole. While the spore is growing the protoplasm disappears, and a clear, refractive material takes its place. When it has reached its full development, the cell-membrane undergoes a gelatinous softening, the cell breaks up, and the spore becomes free. There is usually only one spore to each cell ; as to the nature of its contents nothing is really known. The vitality of the spore is shown by the fact that it will resist a temperature more than double that which suffices to destroy the bacillus. When, however, the spore begins to develop into a bacillus, it loses its tough envelope, elongates, and assumes the appearance of the mother-cell from which it escapes. At this period it is much more easily destroyed even than the bacillus, which when full grown has of course a much stronger membrane than the newly-formed organism. The conditions most favorable to spore-formation are those under which the nutriment for the bacilli has been exhausted and they are about to die. The cells may then leave behind them the seed for a future growth.

Bacteria, like all vegetable cells which do not contain chlorophyll, being unable to obtain for themselves sustenance from inorganic materials in the air or in the soil, grow only where organic material is present for their nourishment. They are to be found where organized life exists, except in the interior of the healthy organs of the body—in the air, in soil, in water, in clothing, on the surface of our bodies, and in the intestinal canal. They grow best in alkaline or neutral media, and multiply, under favorable conditions, with the most astounding rapidity: according to Cohn, a bacterium divides into two in the space of an hour, then into four at the end of a second hour, and into eight at the end of three hours. In twenty-four hours the number will amount to more than 16,500,000. "At the end of two days this bacterium will have multiplied to the incredible number of 281,500,000,000. . . . . The bacteria issuing from a single germ would fill the ocean in five days." Fortunately, the special conditions under which they can grow do not permit of any such rapid development. It is chiefly in dead organic substances that they find this favorable soil. It is now well understood that the process of decomposition is not only accompanied by them, but that through them alone it is also begun and carried on. To quote Cohn again: "Without the activity of bacteria all created things would retain their form and structure after death as well as the Egyptian mummies, or the wrecks sunk in the Dismal Swamp, or the bodies of the mammoth and rhinoceros frozen for untold thousands of years in Siberian ice with uninjured hair and hide."

Those bacteria which are concerned in the decomposition of dead substances of organic origin are called "saprophytic" or "saprogenic" (from *σαπρός*, putrid). A small number, however, grow in the living bodies of higher organisms. These develop at the expense of the tissues, and are, therefore, genuine parasitic organisms, whence they derive their name. Inasmuch as their presence in the body causes a morbid condition, they are generally called "pathogenic bacteria." Most of the parasitic organisms are, however, capable of growing in decomposing matter, and therefore may be saprophytic.

In general it may be said that bacteria develop best at temperatures varying from 30° to 40° C. There is little growth below 20° C. or above 40° C. The saphrophytic forms prefer a temperature of about 24° C.; the pathogenic organisms grow best at or near the temperature of the body.

In studying the fermentations Pasteur discovered that certain organisms could live without oxygen, and these he called *anaërobic*, while others were able to multiply only in the presence of air. The latter he called *aërobic.*

The greater portion of the bacteria are aërobic, a slight diminution in the amount of oxygen being sufficient to prevent their development. Others, however, can grow well in media rich in oxygen, but are able also to grow where there is no oxygen. The latter are sometimes called the "facultative-aërobic bacteria." Most of the pathogenic bacteria belong to this variety. The oxygen in the body, with the exception of the lungs, is not present in large quantities, and what little is found there is soon consumed. As illustrating the action of the two kinds of bacteria, it may be well to give the following summary of Pasteur's theory of fermentation in decomposition:

> The process begins some twenty-four hours before outward manifestations are perceptible. During this time the bacteria (or the microbes, as Pasteur prefers to call them) fall upon the fluid, and the aërobic forms multiply with great rapidity, absorbing all the oxygen in the fluid. Owing to their great numbers, the fluid becomes cloudy. If the fluid is so shut off that oxygen cannot get at it, the aërobic forms die and are deposited at the bottom of the vessel. When all the oxygen is used up, the anaërobic begin to develop, and the process of decomposition advances in a corresponding ratio. If air is admitted, the aërobic organisms form a scum (mycoderma) on the surface, and gradually shut off all access of oxygen, so that the other variety may be able to develop. Mould-fungi may be found in this layer. Two chemical processes are going on in the mean time, owing to the action of the two varieties. The anaërobic cause a fermentation in the deeper parts by changing the nitrogenous compounds into simpler but still complex combinations, while the aërobic, living at the expense of free oxygen, decompose these combinations still further until they are reduced to the simplest binary combinations, water, carbonic acid, and ammonia. Although true fermentation is due to an organism that does not feed on oxygen, yet the process will go on better when free access of air is given, as this provides for the aërobic form, which is essential for the beginning and end of the process. If the decomposition is fully completed, the organisms die, and their remains will be destroyed by other bacteria; and this process will go on until the organic material is completely separated into the constituents of the atmospheric and mineral kingdoms.

Light has also an influence upon the growth of bacteria; that is, the presence of sunlight is distinctly unfavorable to their development.

Very important factors in the etiology of surgical diseases are the *chemical products* of the micro-organism, whether developed inside or outside the body. The saprophytic bacteria, although they are non-pathogenic, may produce powerful poisons by setting up decomposition in necrosed fragments of tissue. As decomposition is not a specific process, but a general expression for a multitude of different chemical combinations, it is not surprising that there should be formed a large number of chemical substances the nature of which is still quite imperfectly understood. Most prominent among those who have studied the substances are Selmi and Brieger, who have given the name ptomaïnes (*πτῶμα*, a dead body) to substances developed during these processes. Absorbed into the body, the ptomaïnes give rise to that class of infection known as "putrid intoxication," or sapræmia. Among the ptomaïnes is the sulphate of sepsin, described by Bergmann. Selmi has described a series of alkaloids obtained from decomposing substances, which alkaloids resemble atropine, morphine, and curare in their physiological action; and Nencki has obtained a substance, the so-called "collidin," which produces a similar effect. Brieger has added to these substances cadaverin, putrescin, and several others. Some of Brieger's ptomaïnes produced the most profound toxic disturbance, and others are more or less harmless. To the former class probably belong the "toxines." The term ptomaïne, however, is now largely used to indicate all products of bacterial growth. Some of these substances have a deleterious influence upon the micro-organisms themselves. During the process of certain fermentations acids are sometimes developed that check further bacterial growth, and the process of fermentation comes to a standstill. More will be said upon this subject, however, when studying the process of infection. Leucomaïnes are animal alkaloids which result from tissue-metabolism in the body independently of bacteria. Their rôle in pathology is not yet well defined.

In addition to the chemical products of fermentation, putrefaction, and infection there may be *pigment-formation*. The organisms which produce these substances are known as "chromogenic bacteria," having been classified by themselves by some writers. They probably do not directly form this pigment, but a basic substance, which subsequently, by contact with oxygen or chemical substances in the media in which the bacteria are growing, produces the characteristic color. Other bacteria produce phosphorescences, but with both of these varieties surgeons have little to do.

The anaërobic bacteria have a decided tendency to produce *gas-formation*, the nature of which is not yet understood. The cholera bacteria when cultivated have a peculiar odor, and those of decomposition may be present even in pure cultures of many forms of bacteria.

We come now to the study of these organisms, but all that will be attempted here will be to give a general idea of the best methods now in use in bacteriological laboratories. For details of this part of the subject the reader is referred to the text-books of Fränkel and Baumgarten in the German language, Cornil and Babes in the French language, and Sternberg's *Manual of Bacteriology*.

Before the *methods* now in use were adopted it was extremely difficult to see the very minute organisms under the microscope. In the process of staining and preparing a thin section everything was done to bring out as clearly as possible the anatomical elements of the tissues. The magnifying power used was sufficiently high for examining cells and fibres; higher powers cut off the light and made the picture obscure. There was obtained by the methods then employed a good view of what is called the "structure picture;" that is, the anatomical structure of the specimen was satisfactorily observed. Now, in order to see bacteria properly, the specimen must be so arranged as to see as little as possible of the structure picture. These details are seen because their refractory power is different from the fluid in which the section lies. If the refracting powers were the same, these objects would not be seen. The elimination of the structure picture is accomplished by the Abbe condenser, which is placed beneath the object and between it and the mirror. In this way many more rays are collected and focused on the object than those thrown by the mirror alone. The field of vision is flooded with light even when very high powers are used, and the structure picture now disappears. If at any time it is desired to make the tissues more apparent, all that is necessary to do is to cut off some of the rays with the diaphragm, and a return can then be made to the conditions which existed when no condenser was used. The bacteria must be colored very deeply or they will also be obscured. The staining fluids in use in 1870 were principally carmine and hæmatoxylin. These fluids stained nuclei well, but they also stained the other elements of the tissue, and had but little if any power to stain bacteria. When the aniline dyes were tried a few years later, it was found possible to color the nuclei of the cells and the bacteria with great perfection. The picture thus obtained is called the "color picture." If now it is desired to obtain the color picture alone, the condenser must be used without any diaphragm, but if it is desired to examine the structure of an uncolored section, if the condenser is used there must be employed the narrowest diaphragm in order to bring out the details.

But it is not always necessary to stain bacteria in order to see them, and they can be examined in liquids also. Supposing it is desired to examine a flask containing bouillon in which bacteria are growing. A platinum loop, previously passed through the flame of a Bunsen burner and allowed to cool, is dipped into the solution, and a minute drop is carried on its point to a carefully-cleaned cover-glass. The fluid must be spread out over the cover-glass so as to form a thin and even film. The glass is then turned over and laid upon the object-glass very carefully, so that no air-bubbles or dry places are allowed to remain. The thinnest possible capillary layer of fluid should lie between the two glasses.

If the organisms to be examined are growing on a solid culture-soil, a drop of distilled water is first placed on a cover-glass, and a small fragment of the culture is removed on the point of the platinum needle and rubbed up in the water. The glasses are arranged as before: a high power and immersion must be used with a medium diaphragm. The bacteria will be seen moving about in the liquid. This method is used chiefly for the purpose of determining whether a specimen contains micro-organisms or not. The liquid cannot be preserved for any length of time, for it soon dries up. The "hanging-drop" method obviates this difficulty. A drop of the fluid is obtained by a loop with due precautions, and is placed upon the centre of the cover-glass. A little vaseline is painted around the outer border of the cover-glass, which is then turned over and placed upon a hollowed-out object-glass. The vaseline seals up the chamber thus formed. Dry cultures can be examined in this way as well as fluid cultures. The fewer organisms there are in the drop the better. The border of the drop is the best part to study, as many bacteria will become attached to the edge of the drop, and will not, therefore, be so active in their movements. The form and size of the bacterial cell can well be studied in this way, and the preparations can be preserved for some time, cultures being taken from them later. The principal object of this method is to study the motility of the bacteria.

The commonest way of examining bacteria is by some one of the usual *staining methods*. It is well to remark here that most varieties of organisms have not any special staining reaction peculiar to themselves, but can be stained by the ordinary cover-glass and aniline-dye method.

The aniline dyes are derived from coal-tar products. Those most frequently used are the basic dyes, such as gentian-violet, methyl-violet, methyl-blue, fuchsin, and Bismarck-brown. The element in them that holds the coloring matter is of a basic character. The acid dyes, as eosin and acid fuchsin, are used to obtain a diffused contrast stain in the tissues.

With the basic dyes an excellent "color picture can be obtained." The acid dyes bring out not only the nuclei of the cells of the tissues, but their protoplasm also, and therefore produce more of a "structure picture," while the bacteria are hardly stained at all. The dyes seem to color the bacteria by virtue of a chemical action. They are usually dissolved in concentrated alcohol by shaking up an excess of the powder in alcohol and allowing it to stand and settle, and the fluid is then filtered immediately before use. These solutions are kept on hand and are diluted for use. A flask should be filled two-thirds with distilled water, and the alcoholic solution is then added drop by drop, as long as the fluid in the flask remains transparent.

Gentian-violet is a strong and very desirable coloring agent, but it can easily overstain.

Methyl-violet is less powerful, but also less durable.

Fuchsin is one of the finest coloring agents: it does not overcolor and is very durable.

Bismarck-brown, which colors slowly, is usually employed as a diffuse stain, and it would probably not be used at all except that it is very suitable for photography.

Many of the dyes can be reinforced and finer details can be brought out when desired by the addition of mordant substances, such as alum and carbolic acid. Ziehl's solution, used for this purpose, consists of the following ingredients:

Fuchsin,	gm.	1.
Alcohol,	c.c.	10.
Carbolic acid, 5 per cent. solution,	c.c.	90.

Heating the solution during the staining process also makes the coloring more intense and durable. A high degree of heat is, however, not suitable for sections, but rather for dried specimens on the cover-glass, as will presently be seen.

If the preparation has been too deeply or generally stained, the excess can be removed by washing out in water or in alcohol. A weak solution of acetic acid may be employed for this purpose.

One of the best ways of demonstrating the presence of bacteria in tissues is that known as "Gram's method." The preparation is first placed for one or two minutes in a solution of gentian- or methyl-violet in aniline-water. It is then placed for one minute in the following solution: iodine, 1 part; iodide of potash, 2 parts; distilled water, 300 parts. This solution forms with the dye a deposit confined entirely to the bacteria. The preparation is now placed in absolute alcohol until it appears colorless to the naked eye. The alcohol is removed with blotting-paper, and the specimen is finally mounted in Canada balsam. This is considered one of the best methods of staining for those bacteria which it does not decolorize. If desirable there can now be obtained a staining of the tissues with carmine or eosine, and thus "a double staining" be accomplished, the bacteria being of a deep-blue color, while the tissues have the contrasts which the different shades of red afford. This method, though difficult in execution and inapplicable to many forms of bacteria, gives excellent results in those cases to which it is adapted, and the inability of a bacterium to take this stain is often of diagnostic value.

Supposing, now, it is desired to examine the blood, or the juices of internal organs, or sputa for bacteria, or a culture, and to employ the staining process—for uncolored preparations are of little or no use to the bacteriologist—the first step is to spread out a minute portion of the substance, as has already been shown, upon the cover-glass with a sterilized platinum needle. To make the layer as thin and even as possible a second cover-glass is placed over the first and the two glasses rubbed gently together. When separated by carefully sliding apart the glasses afford two preparations. They must now be laid down with the specimen uppermost, and be protected by a bell-glass while drying. One of the great difficulties in staining such a dried specimen is that, as soon as the dye is allowed to come in contact with it, the albuminous portions, if such are present, swell up and become fluid again, and precipitate particles of colored matter which ruin the preparation. This is overcome, however, by heating the cover-glass by passing it through a flame of a Bunsen burner three times quickly, the preparation being uppermost. This heating does not seem to interfere at all with the form or with the staining power of the bacteria, and it fixes the specimen upon the cover-glass. The coloring fluid selected is next dropped upon the specimen, which is afterward washed in distilled water, and the specimen is now ready for mounting. The preparation may be made upon the slide instead of upon the cover-glass, and be examined without the intervention of any cover-glass. This gives greater facility of manipulation, and the slide can readily be cleansed if a permanent specimen is not desired, but, if this be done, great care must be taken of the lens.

There are one or two modifications worth mentioning. If it is desired to remove any hæmoglobin present, the glass should, after drying, be placed for a few seconds in a 1 to 5 per cent. solution of acetic acid, and, after washing in distilled water, be dried again before staining. If it is desired to clear up the specimen so that the cells shall not be visible under the microscope, there can also be used the acid, or, better still, two or three drops of a 33 per cent. solution of potash or soda in a watch-glass of distilled water. This leaves the contours of the nuclei still faintly visible. Masses of fat are undesirable in such specimens for they confuse the picture and are likely to give deceptive imitations of bacteria, owing to the crystals which form. This material is disposed of by heating the cover-glass after allowing a drop of the dilute potash to fall upon the specimen. The fat is then dissolved and becomes invisible. The same purpose can be effected by dipping the specimen in chloroform and afterward in alcohol. The specimen, when satisfactorily prepared, may be mounted in water, and Fränkel strongly recommends this to be done, as the shape of the bacteria is thus preserved and their membranes are better shown. If it is necessary to mount them in a permanent shape, the specimens can be placed in Canada balsam, dissolved in xylol rather than in chloroform, as the latter robs the bacteria of the coloring matter and the specimen quickly fades.

It is exceedingly difficult to stain spores. By the ordinary methods of staining spores remain uncolored and appear as highly-refractive bodies, which are better seen in recent cultures, owing to the contrast with the highly-colored protoplasm of the young bacilli. Spores may, however, be stained if they are exposed for some time to heat. The cover-glass containing the specimen to be stained may be placed in a hot-air oven at a temperature of 120° C for an hour, or at a higher temperature for a shorter time, or it may be passed eight or ten times through the flame of a Bunsen burner. The spores may then be stained with an aqueous solution of fuchsin or methyl-violet. This method so injures the bacilli that they do not color as well as usual. If a double staining is desired, Möller's method may be used.

According to Möller, the material is placed on a cover-glass, and is allowed to dry; it is then passed three times through a flame, or is left for two minutes in absolute alcohol; it is then placed in chloroform for two minutes and washed in water, and afterward from half a minute to two minutes in a 5 per cent. solution of chromic acid, and again washed in water; a solution of carbolic fuchsin[1] is now poured over the glass, which is heated in a flame until boiling occurs for sixty seconds, when the solution is poured off and the preparation is decolorized in a 5 per cent. solution of sulphuric acid and washed in water. It is next placed in an aqueous solution of methylene-blue or of malachite-green, and again washed in water. The preparation is now dried and mounted in balsam. The spores are stained dark red, and the protoplasm of the bacilli is blue or green.

To prepare pathological specimens for bacteriological study the portions to be examined should be cut into pieces about half an inch square and placed in absolute alcohol. The alcohol must be changed once or twice, and at the end of a few days the specimens are ready for the section cutter.[2] The sections can be taken out of water or alcohol and placed in a dilute coloring fluid for from five minutes to an hour or more. They are then placed in acidulated water or in 60 per cent. alcohol to remove the excess of coloring matter; they are washed afterward in water, which must be removed by alcohol before placing the sections in oil of cloves, or, better, in oil of cedar, whence they are taken and permanently mounted in Canada balsam. If a section is overstained, washing in alcohol will remove the superfluous color better than water. Alcohol is sometimes too powerful in its bleaching effects, and it is therefore desirable to remove the water by evaporation before placing the section in oil. If it is desired to make a double staining, Bismarck-brown in weak solutions or picrocarmine may be used. Fränkel thinks it is better to reverse the process; that is, to stain the nuclei first and the bacteria afterward. It requires considerable experience to distinguish readily all objects which are of non-bacterial origin, but closely resembling micro-organisms.

Examination with the microscope alone would not have accomplished a great deal in the science of bacteriology. It was necessary at first, in order to preserve live bacteria for study, that a medium should be provided in which they could grow. Although Pasteur accomplished a great deal with his bouillon culture-fluids, it was found that there were certain disadvantages inherent in this method of investigation that offered obstacles to further progress. The facility which a fluid offers for indefinite growth in every direction makes it exceedingly difficult to separate the different varieties of bacteria from one another. This differentiation was attempted by taking an exceedingly small quantity from one flask and placing it in a fresh flask, and later repeating the same opera-

[1] See page 57, Surgical Bacteria. [2] See Appendix.

tion, until finally the dilution was so great that but one organism was found in each drop, and the special form was thus obtained. The slightest error in the process, however, speedily reproduced an impure culture. It was Koch's great merit to have systematized the first rude attempts to grow bacteria on solid culture-media and to bring the art of culture to its present state of excellence, though undoubtedly we are as yet but upon the threshold of this new field of science.

The great advantage of the *solid-culture method* lies in the opportunity which it gives to isolate the different varieties of bacteria from one another. Having accomplished this, bacteria can now be planted rapidly from fresh growths until the organism has passed through several generations, with the certainty that there will result a growth which is not only a particular kind of bacteria, but one that has now become entirely disassociated from the orignal source from which it was taken. To provide a suitable soil the soil must not only contain those ingredients which bacteria need for their growth, but it must also resemble, as nearly as it can be made, the chemical constitution of those tissues which the organism attacks. It is also absolutely necessary that the material used must entirely be free from organisms of any kind, and that it must be sterilized thoroughly. For fluid culture-media a watery extract of meat or a bouillon is used; for the solid culture-media an admixture of gelatin, or a Japanese substance known as "agar-agar," or coagulated blood-serum, potato, or egg-albumin, etc., is employed.

Sterilization of culture-media is a most important feature of bacteriological technique. It may be effected by heat or by filtration. The former method is the one chiefly employed.

Bacteria which do not form spores are killed at a comparatively low temperature. Sternberg found that the pyogenic cocci required the highest temperatures, and that they were killed by an exposure for ten minutes to a temperature of 62° C. All bacteria are destroyed in one or two minutes, in the absence of spores, by exposure to the action of boiling water or of steam. A very much higher temperature is required for the destruction of micro-organisms when dry heat is used. The spores of bacilli have a much greater resisting power, and in some cases are not destroyed by a boiling temperature maintained for several hours; but the majority are killed by being subjected to the boiling temperature of water for a few minutes. *Fractional sterilization* is employed for certain nutrient media, for the reason that prolonged boiling may injure them.

This method is based upon the supposition that some of the more resistant spores may be present in the culture-material, and that bacteria may be developed from them after sterilization by the ordinary method. A repetition of the process will therefore destroy the growing bacteria which are developed from such spores. The culture-material is subjected for a short time to the temperature of boiling water; after an interval of twenty-four hours the operation is repeated for the purpose of destroying those bacteria which may have developed in the mean time from spores. This is repeated at corresponding intervals from three to five times.

Test-tubes and all glass and metal objects which it is intended to use in the laboratory are sterilized by *dry heat.* A hot-air oven made of sheet iron with double walls and shelves is used for this purpose. A much higher temperature is needed under these conditions than when moist heat is used. Micrococci and bacilli are not destroyed below a temperature of 120° C. It is necessary to raise the temperature to 140° C. to destroy spores, and the degree of heat should be maintained for an hour or more. When, therefore, apparatus is sterilized, a temperature of about 150° C. should be maintained for this length of time.

FIG. 1.—Arnold Sterilizer.

As moist heat acts more rapidly upon bacteria, the *sterilization by steam* is extensively used. Koch's apparatus consists of a copper or a zinc cylinder which is covered with a jacket of felt. There is an opening at the top for the escape of steam, and another through which a thermometer may be inserted. The water in the cylinder is heated by a Bunsen burner, and the steam is maintained at a temperature of 100° C. Near the lower third of the vessel is a perforated shelf which is placed sufficiently high so as not to come in contact with the water. The Lautenschläger sterilizer is so arranged that a current of steam descends from above upon the objects to be sterilized and passes out through the bottom of the vessel. The Arnold sterilizer (Fig. 1), which is largely used in the United States, is convenient, as it is so arranged that steam can be obtained rapidly with a small quantity of water. It has the advantage also of great simplicity. The autoclave is a form of sterilizer by means of which steam can be obtained under pressure. Under these conditions a single sterilization at a temperature of 115° C. for half an hour suffices. This apparatus is, however, expensive.

Test-tubes which are to contain the nutrient media are plugged with cotton, which acts as a filter, allowing the access of air, but preventing the entrance of bacteria. After sterilization in the hot-air oven the tubes are ready to be charged with the nutrient media. The bouillon peptone-gelatin is subjected to a temperature of 100° C. for ten minutes at intervals of twenty-four hours, four days in succession. Bouillon and agar-agar jelly may be prepared in the same way or be steamed once for an hour. The sterilization of culture-material should be tested by placing it for a few days in an incubating oven at 30° to 35° C.

The culture-media should be slightly alkaline, and should resemble as closely as possible the fluids of the body.

To make a suitable bouillon, cut up 500 grammes of lean meat, place it in a pint of water, and let stand for twelve hours in a cool place. Now squeeze through a loose cloth, a little peptone being then added to take the place of albuminous substances precipitated on heating. Boil in a water-bath or in steam three-quarters of an hour, and neutralize with a saturated solution of the carbonate of soda. Boil again one hour, and the coagulable albuminoids will be precipitated or will float upon the surface. Filter through paper wet with distilled water. The bouillon must still be kept alkaline, or at least neutral, and should not, after repeated boiling, become in the least cloudy. The white of an egg, added before boiling, helps to clear up the fluid. The fluid thus prepared should be placed in sterilized test-tubes, and the tubes thus charged must finally be sterilized by the fractional process.

Bouillon is a good material to use if it is desired to measure a given number of bacteria, as each drop will always have about the same number, or if it is desired to watch their development in the hanging drop or to obtain large numbers of bacteria. One of the first forms of *solid media* used was the cut surface of cooked potatoes.

FIG. 2.—Potato-culture.

A practical method for preparing potatoes for planting bacteria is as follows: Good-sized potatoes should be selected, and the ends sliced off. They are then punched with an apple-corer. Cylinders about two inches in length are thus obtained, which are split obliquely. These pieces are allowed to soak in cold water for two or three hours, and are then placed in sterilized test-tubes containing a fragment of glass to support the potatoes in such a way that they will not be immersed in the water of condensation. The tube thus charged is sterilized by the fractional method (Fig. 2).

Gelatin possesses the much greater advantage of providing a solid material which is at the same time transparent.

Nutrient gelatin should thus be prepared: 1000 parts bouillon, 10 parts peptone, 5 parts salt, 100 parts gelatin are the proportions of the ingredients. Shake and heat to melt the gelatin. Soda solution should be used for neutralizing. Boil the mixture half an hour to precipitate coagulable substances, and filter. The filter must be warm. The resultant fluid must be clear, and must remain so on boiling. In sterilizing it must not be subjected too long to heat, as heat injures the stiffening properties of the gelatin. Steaming fifteen minutes a day for three days is sufficient.

The disadvantage of gelatin is its liability to become softened by heat, and it therefore cannot be used for making plates of those organisms requiring for their development a temperature of 30° C.

Agar-agar is a substance resembling isinglass, prepared in the far East from a gelatinous form of algæ. It is nearly soluble in hot water, forming a jelly which melts only at 90° C. and hardens again at 40° C. The preparation of agar is much harder than that of gelatin, on account of the greater difficulty of filtration. The addition of 6 to 7 per cent. of glycerin to the preparation makes it a suitable soil for the growth of tubercle bacilli.

Agar-agar is thus prepared: To 100 parts bouillon, 10 parts peptone, and 5 parts salt are added 1 to 2 parts agar-agar. This mixture must be boiled for two or three hours before filtering.

Blood-serum may be employed for the growth of a great variety of bacteria, but more particularly for those organisms which do not develop readily on other media. The blood is received in sterilized cylinders, which remain on ice for two days to allow the coagulation to be completed. The serum is then removed with sterilized pipettes and placed in test-tubes. Human serum, ascitic, hydrocele, and ovarian fluids have been used in the same way.

The tubes thus charged are sterilized by the process of discontinuous heating. They are left in a hot-water bath of a temperature of 60° C. for about an hour daily for from five to seven days. Koch has devised an apparatus for this purpose. The tubes are left in an oblique position, so that a large surface may be exposed for culture purposes. After being sterilized the serum is solidified by a careful exposure to a temperature of about 68° C., which causes it to coagulate, forming a transparent jelly-like mass.

A great many forms of organisms will not grow upon any of these culture-soils or on any that are now used. This can easily be demonstrated by trying to inoculate them with a drop of saliva which under the microscope can be seen to contain a great variety

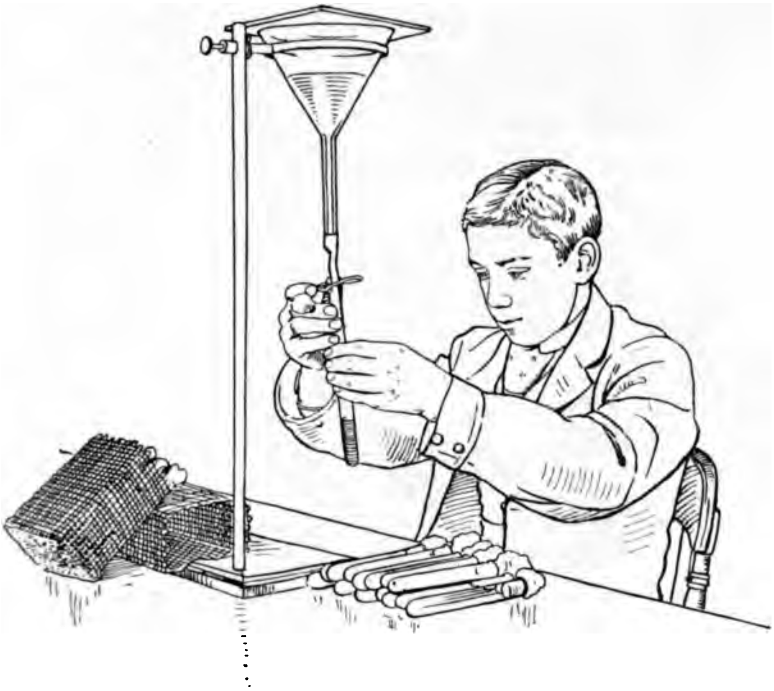

FIG. 3.—Method of Filling Test-tubes with Nutrient Material.[1]

of organisms. The resulting culture will contain but comparatively few of these forms. About 10 ccm. of the culture-media are placed in each test-tube. The gelatin is allowed to harden with the test-tubes in the vertical position, and is inoculated by thrusting the platinum needle, charged with the infected material, into the gelatin. This is the so-called "stab-culture" or "stick-culture." The agar-agar and blood-serum are usually allowed to solidify while the test-tube is in an oblique position, thus giving as large a surface as possible for the bacterial growth.

If, now, there is a great variety of bacteria growing in a speci-

[1] The funnel containing the material to be used is protected from the air by a plate of glass. A rubber tube connects the funnel with a pointed glass nozzle, and the flow of fluid is controlled by a Mohr check-cock. A plug of cotton is held between the fingers of the right hand, and the tube is held in the left hand. On the right are the empty sterilized tubes, and on the left are the baskets containing the tubes which have been filled.

men (as in fæces), they can be separated by *plate-cultures*. Three test-tubes containing the gelatin mixture are melted in a water-bath at a temperature of from 30° to 40° C. : a very minute fragment of the material to be examined is placed in one of the tubes, and is thoroughly mixed with the culture-fluid ; from this "original" tube, as it is called, three drops of the liquid are transferred to the second tube, and from the second tube three drops are transferred to the third. The culture-fluids are thus progressively made more dilute. The fluid gelatin is poured into Petri dishes (Fig. 4) or upon square glass plates, and is allowed to harden. The plates are then placed in a large double dish upon little trays, one above another. Wet filter-paper is placed in the bottom of the dish to keep the air moist. The bacteria in the fluid are thus more or less widely separated from one another, and the various colonies are given an opportunity to develop separately. There is thus an opportunity not only to determine the number of varieties, but also to contrast them with one another. Some liquefy the gelatin ; some are pigmented. If it is desired to examine a particular colony, the plate containing this growth may be placed under a microscope of low power, or, under favorable circumstances, a cover-glass may be placed upon the colony and the oil immersion may be used ; or the cover-glass with the adherent colony may, after removal, be dried and stained in the usual manner. Many bacteria that cannot be separated in any other way may be obtained by the plate method.

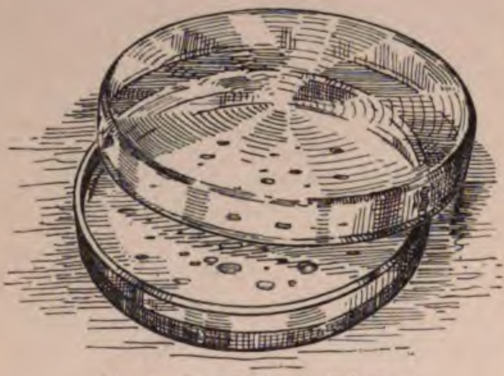
FIG. 4.—Petri Dish with Colonies.

The colonies it is desired to study must now be transferred to culture-tubes, where they are more protected from infection from outside sources and can more carefully be studied. A minute fragment is taken from one of the colonies while observing it through a lens of low power. The needle with the fragment thus obtained is thrust deeply into a gelatin culture-tube. As the culture grows it is not difficult to determine whether it is pure or not. Another mode of transferring the culture from the plate is to draw the platinum needle over the surface of the agar-agar, which is usually allowed to harden by placing the tube in an oblique position. This allows the culture to grow upon the surface and in the presence of oxygen. As a rule, the gelatin and agar cultures will live for three or four months; it is better, however, to renew the cultures every six weeks.

The anaërobic bacteria are much more difficult to cultivate. The culture-media must be treated with substances which rob them of their oxygen. The organisms must thoroughly be mixed with the gelatin. After spreading the fluid gelatin containing these organisms on plates, they are covered, before hardening, with thin leaves of mica to cut off the oxygen, and are sealed up by paraffin poured over the edges of the mica. Or the gelatin may be boiled in the test-tube before the bacteria are mixed with it, and then quickly hardened. The boiling process drives out the oxygen, and the deeper layers in the tube are protected from oxygen by the upper layers, and anaërobic bacteria can then be made to grow. This method, which has the advantage of supplying different amounts of oxygen, is available for those anaërobic forms that can grow where there is no oxygen, but prefer oxygen. They will be found in the upper layers of the tube. Those which can only grow where there is no oxygen will be found at the bottom of the tube.

If the gelatin in a tube is punctured by a platinum needle armed with anaërobic bacteria, the deeper portions only of the puncture line will show signs of growth; as the layers are reached where oxygen still exists, the growth will stop. Eggs may be used for the same purpose. A small puncture having been made and the organisms introduced, the hole is sealed up with collodion. The small amount of oxygen existing in the egg is soon replaced by sulphuretted hydrogen. A method of cultivating anaërobic bacteria in the presence of hydrogen gas will be described in connection with the tetanus bacillus.

If it is necessary to keep the culture medium at a high temperature, an oven must be provided for the purpose. That now generally in use has a double wall which contains water heated by a gas-jet. The degree of heat is indicated by a thermometer and is regulated by some automatic arrangement. The escape of heat from the sides of the oven is prevented by a felt jacket.

The action of the pathogenic bacteria in disease is not yet fully understood. One of the earliest theories assumed that the presence of bacteria in large numbers in the organs acted mechanically to impair their functions. This is probably true to a limited extent only. According to Fränkel, their action is explained by the development of a specific, exceedingly poisonous substance having a very deleterious influence upon the organism. This poison, like that of the serpent, may spread itself all through the body, and, although small in quantity, may produce very marked effects. It probably varies greatly in amount in different cases.

As to whether the poison is a product elaborated from the bacterial cells as a specific excretion, or is the result of a tissue-metamorphosis brought about by the organisms, which select from the tissues such substances as are most nutritious to them, is a point about which authorities differ. Opinions at the present time are pretty evenly divided upon this point. It can easily be understood that when one or two important elements are taken from the chemical composition of a cell or from the matrix in which it lies, an entirely new chemical compound may be the result. The chemical nature of the tissues in which the bacteria grow is therefore an important element in determining the nature of the compound that will be formed. It is a well-known fact that the albuminoids, for instance, are necessary for the development of most toxines. Poisonous substances may be developed in one case which in another fail to form, owing to the absence of some important basic substance.

The result of such action of bacteria upon the cells of the body is to produce what is known as "irritation." If the action is sufficiently powerful, death of the cell will ensue, but if it be less powerful and continued for a certain length of time, the result will be a growth of new cells. This action is probably exerted through the endothelium of the capillaries, for we often see bacteria enclosed within such cells. These cells exercise an important influence upon the nutrition of the organ, as they determine to a certain extent what chemical substance shall be allowed to pass through the vessel's walls for its nourishment. The result of such a disturbance of nutrition upon the organ will of course affect its functions, and this may go to the point of producing all the phenomena of an inflammation. The production of a general constitutional disturbance will be found discussed at more length in another chapter. It may merely be said here that the most generally received opinion is that substances are produced which have a ferment-like action and increase the tissue-metamorphosis greatly throughout the body. Baumgarten, however, believes that the growth of foreign organisms in the body is alone sufficient to account for all the phenomena of fever without assuming development of a particular virus.

It is a well-known fact that ptomaïnes can be separated from their bacteria, and, if introduced into the body, can produce local or general disease. That apparent suppuration can be produced experimentally in this way has finally, after much discussion, been determined in the affirmative. Introduced in large quantities, ptomaïnes may excite grave constitutional disturbance. These substances are not, however, multiplied and reproduced within the body; they exert only a passive rôle. Such a condition is known as "intoxication" or "toxic infection," as distinguished from the "septic infection" of bacteria.

The question of immunity of the living body to the action of certain bacteria is one which has received a vast amount of attention, and is still unsettled. Leading up to this question is that of the mitigation of the virulence of bacteria and the production of a vaccine, as first broached by Pasteur. This change in the activity of the organisms may be produced by allowing them to grow for an unusually long time in their culture-media. In this way the power to develop in the living body seems gradually to be lost. This change in the bacteria shows itself in a more vigorous growth upon the soil than took place at first, when it was less accustomed to its situation. The organisms of chicken cholera and anthrax were first successfully cultivated so as to produce a "vaccine" for these diseases.

Another way of weakening the action of the bacteria is to mix with the culture-media certain chemical substances which are poisons to them, but not sufficient in amount to kill them. Roux weakened the anthrax bacillus in this manner by mixing bichromate of potash with the bouillon. This experiment suggests an explanation of the cause of the insusceptibility of certain animals to some forms of bacteria which are passed through them, owing to the presence of peculiarly hostile chemical compounds in their blood. A weakening of their power is also brought about by exposure to atmospheric pressure, sunlight, and high temperatures. The cause of the weakening of virulence is supposed to lie in a degeneration of the bacterial cell-protoplasm, but there is no marked change visible to the eye.

How far this process of protective inoculation can be carried in the control of disease is a very doubtful question, but the fact has been definitely established that under certain circumstances a mitigated virus can render the most virulent poison harmless. Bitter has shown that the bacilli of the anthrax vaccine develop only in the immediate neighborhood of the point of infection. Heuppe and Wood were able to produce the same immunity to anthrax by the injection of organisms, quite of a different nature,

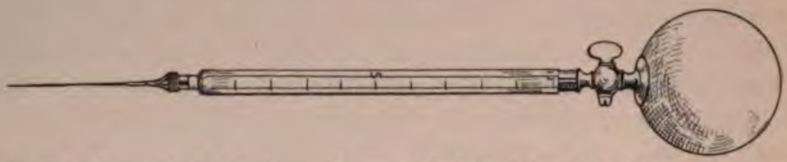

FIG. 5.—Bacteriological Syringe. On removal of the rubber bulb this instrument can be sterilized by dry heat. The almost capillary lumen permits great accuracy of dosage (H. C. Ernst's modification of the Koch syringe).

and not even pathogenic, into animals which ordinarily were very susceptible to the disease; and the same immunity has been produced by the injection of peculiar forms of albumin in no way connected with bacterial growth. According to Fränkel, the protection afforded by vaccination is therefore the result of many substances which are chiefly of bacterial origin. According to Pasteur, immunity is acquired by the exhaustion of a chemical substance necessary for the growth of the micro-organisms. The "retention" hypothesis assumes that the products of tissue-metamorphosis remain behind after the first invasion, and prevent a return of the same kind of organism. According to Fränkel, this hypothesis has fewer objections than any other. It is known that in some forms of fermentation substances are developed which prevent the further growth of organisms, and may even prove poisonous to them.

The *phagocyte theory of Metschnikoff* is still exciting great attention, and although it has already been referred to in another chapter, an allusion to it in this connection cannot be avoided.

The first studies were made upon the Daphniidæ ("water fleas"). The needle-shaped organisms which invaded the intestinal canal and the tissues of its body were surrounded by leucocytes and taken up into their protoplasm, and there were changes thus produced in them which suggested a sort of digestive process. Metschnikoff also placed fragments of liver taken from a rat, dead of anthrax, under the skin of a frog, and found them later infiltrated with leucocytes in whose protoplasm many of the bacilli were found. He found also that the bacilli, when artificially weakened and injected into warm-blooded animals, were quickly taken up by the leucocytes, but when injected with their full strength still preserved, only a few were found in the spleen thus enclosed by leucocytes. He accordingly advanced the theory that the leucocytes, like their ancestors, the amœbæ, had a certain instinctive propensity, in search of material for their nourishment, to consume the invading organisms. Hence the term "phagocyte." The protective influence of vaccination was supposed by this observer to be due to the power which the consumption of weaker forms of bacteria gave to the leucocytes to devour the more virulent varieties. The opponents of the phagocytosis theory, who are numerous, claim that the phagocytes eat up the bacteria only when the latter have been killed by other influences. It should be mentioned that the leucocytes are not permanent bodies, therefore a capacity on their part for transmitting this acquired power to their descendants must be assumed if this theory is adopted.

Although the phagocyte theory seems to play a certain rôle in the problem of immunity, the general weight of opinion seems at present to be opposed to this very attractive theory in its entirety, and to lean to the view that predisposition to disease means a favorable culture-soil for the bacteria in question, and immunity from disease means a soil unfavorable to those organisms. The chemical constitution of the blood-serum is therefore probably a more important factor in resisting or in favoring the invasion and growth of bacteria than any peculiar powers possessed by the white blood-corpuscles.

When it is realized how hard it is to cultivate certain forms of bacteria on artificial media, it does not seem surprising that the varying condition of the chemical constitution of the blood and tissues of different animals, or the changes occurring at different periods of life of the same individual, should produce soils at times unfavorable to the growth of pathogenic bacteria.

Buchner thought that this destructive power of the blood-serum lay in the amount of salts it contained and the albuminates with which they are combined. If, for instance, a rat is treated with phosphate of lime, which causes a production of acid in the body, the high grade of alkalinity of the blood will disappear and the animal will become susceptible to the anthrax bacilli. If a large number of bacilli are injected into the same kind of animal, a similar result will follow, for, although many of the bacilli are killed by the unfavorable conditions they meet with in an insusceptible animal, the dying organisms liberate acids and pave the way for an invasion of the system by the survivors. It should not be forgotten that an antagonism exists between the healthy living tissues of the body and bacteria. If these organisms gain an entrance into the circulation, they usually disappear rapidly. It was at one time supposed that they were excreted with the bile or the urine, but this is now known not to be the case; for it is established that an uninjured membrane will not allow the bacteria to pass through it, as a rule. Wyssokowitsch found that they were deposited chiefly in three organs, the liver, the spleen, and the bone-marrow. If, on the one hand, the organisms are non-pathogenic, they are destroyed in these organs; on the other hand, if they are pathogenic, they have an opportunity to develop in those localities. There are three routes through which bacteria can obtain an entrance into the body: First, through the skin, generally through some wounded surface, although it has been shown by Garré that the apparently uninjured skin does not offer an insurmountable barrier; secondly, through the digestive canal; and, thirdly, through the respiratory tract.

The pathogenic bacteria may be defined as those which stand in a causal relation to certain well-marked morbid conditions, and they are regarded as the specific agents which produce the pathological symptoms.

Koch lays down as a crucial test that certain conditions must be fulfilled before it can positively be asserted that a given organism is the specific cause of a disease. These are: it must be found in all cases of that disease; it must be found in no other disease; and it must appear in such quantity and be so distributed that all symptoms can be accounted for by its presence; also, that the bacteria must be capable of being isolated from the diseased tissues and be grown upon some of the artificial culture-media, and when injected into an animal must be capable of reproducing the disease. Although all these conditions cannot be fulfilled, yet the constant presence of a single variety of bacteria in a given disease renders it highly probable that it is the cause of the disease.

II. SURGICAL BACTERIA.

THE number of bacterial forms found in, and fully identified with, surgical diseases is not large, yet it can safely be said, from the present standpoint of our knowledge, that the traumatic infective diseases are all to be accounted for by the action of micro-organisms in the tissues.

The organisms which surgeons have most frequently to contend with are those which produce suppuration. Of these there are several varieties, although the majority of them have the globular or coccus form and are called "pyogenic cocci."

FIG. 6.—Staphylococcus Pyogenes Aureus.

The staphylococcus pyogenes aureus was first recognized by Ogston and Rosenbach, the latter of whom gave it the prefix derived from σταφυλή (a bunch of grapes), owing to the characteristic grouping of the cocci in clusters (Fig. 6). Its shape is globular, and the developed organism measures about 0.7μ in diameter. The younger cocci are somewhat smaller, the size depending to a certain extent also upon the nature of the soil in which they are growing. They multiply by division in the manner already described, but the line of fission is difficult to see, owing to its fineness. They are readily stained by all the coloring agents, being well adapted to the Gram method of staining, and being one of the varieties of micro-organisms most easily demonstrated in this way. Although no spores are found, the aureus is a very durable form of organism. Its power of growth is not destroyed by drying for ten days. It requires strong chemical substances or boiling for several minutes in water to kill it. On gelatin-cultures it can preserve its vitality and power of reproduction for a year. Becker first obtained growths of the staphylococcus on gelatin, to which it had been transferred from the abscesses of cases of osteomyelitis, but Rosenbach was the first to recognize that it was not confined to this disease alone, but was common to all forms of suppuration. It grows well at ordinary house-temperatures, but is more active when subjected to a temperature of from 30° to 37° C. It can develop activity in media which have only a very small amount of oxygen. The staphylococcus pyogenes aureus exhibits, when grown upon solid culture-media, certain peculiarities which distinguish it from all other varieties of cocci. When the gelatin is inoculated, a growth of an opaque gray color takes place along the whole length of the puncture. At the same time the gelatin immediately around the growth begins to liquefy, but more rapidly near the surface than lower down. At the end of three or four days the surface of the gelatin becomes completely liquefied, and the bacterial growth begins to sink as the softening of the gelatin proceeds downward. By this time it begins to assume a golden-yellow or orange color, and collects in a mass at the bottom of the puncture-canal. It has a peculiar odor of sour paste, particularly when grown on potato.


FIG. 7.—Staphylococcus Pyogenes Albus.

When a culture is made on the surface of obliquely-hardened agar there forms along the needle track primarily a moist glistening growth, which is at first a yellowish-white, but soon becomes an orange color (Fig. 6). The growth is somewhat elevated above the surface, is from 3 to 4 mm. wide, and has a wavy border. The color may not develop at first, but it appears especially brilliant if the growth has not taken place in the high temperatures of the oven: in the latter case the luxurious growth appears to interfere with the pigment-formation, which occurs most pronouncedly when the growth is well exposed to the air. It can be prevented from occurring if the air is shut off by a film of sterilized oil or by other means.

The aureus is found abundantly outside the human body. Its presence has been demonstrated in dirty dish-water, in the soil, and also floating in the air, particularly in foul hospital wards. But its commonest seat is the superficial layer of the skin. It has been found also in the respiratory and digestive tracts, in the normal mucus of the pharynx and the saliva, in the biliary ducts and the fæces, and, most important of all for the surgeon to remember, in the dirt collected under the ends of his finger-nails.

The liquefaction of the gelatin appears to be due to the presence of a soluble peptonizing ferment which is excreted by the aureus. It has also the power to peptonize albumin. It has generally been supposed that poisonous ptomaïnes and toxines were not formed by the staphylococci, but recent investigations have shown the contrary to be the case. The pathogenic qualities of the cocci of suppuration are described in another chapter. The aureus is the commonest of all pyogenic cocci, and it has been found in 80 per cent. of the cases of suppuration examined.

Staphylococcus pyogenes albus (Fig. 7) behaves in all respects like the aureus, except that it does not develop the golden-colored pigment. It appears to be a variety of the aureus, but cannot be so cultivated as to change into the aureus. It always retains its characteristic white growth, occurs less often than the aureus, and does not seem quite so virulent, as the symptoms caused by it appear clinically less pronounced in severity.

FIG. 8.—Streptococcus Pyogenes.

Staphylococcus viridis flavescens occupies an intermediate position between the aureus and albus (Babes). On agar it forms a delicate film. The cocci are irregular in shape, and are larger than the aureus. The staphylococcus flavescens is very rare.

Staphylococcus pyogenes citreus, a variety seen by Passet in two cases, appears in all respects similar in its behavior to aureus and albus, except that it develops a lemon-yellow pigment. It liquefies gelatin more slowly than the two varieties above named.

Staphylococcus cereus albus et flavus are two unimportant varieties of pyogenic cocci, also described by Passet. The cocci are characterized by a dull, waxy growth on the surface of gelatin. They cannot be distinguished under the microscope in any way from the other varieties. As they are very rare forms, and later observers have failed to find them, Baumgarten suggests that it may be possible the genuine pyogenic coccus had died out, and that the cereus was a remaining form which Passet accidentally observed.

Micrococcus pyogenes tenuis is a name given by Rosenbach to another rare form of pyogenic coccus. It has only been seen once since by later observers. Microscopically, the cocci are somewhat more irregular in shape and larger than those of the aureus. On the surface of agar the tenuis forms a very thin, transparent deposit. This coccus obtains its name from the great delicacy of its growth. It is quite possible that this variety, like the cereus, was an accidental inhabitant of an abscess and not the genuine pus-producer. Rosenbach does not place it among the staphylococcus group of micrococci.

FIG. 9.—Streptococcus Pyogenes (culture).

The *streptococcus pyogenes* is one of the most important varieties of the pyogenic cocci. It usually occurs alone, but sometimes it is found with staphylococci, and is microscopically identical with the streptococcus of erysipelas. The arrangement of the cocci distinguishes it in a marked degree from the staphylococcus group. The cocci are arranged in rows or chains (Fig. 8), instead of in bunches. There are usually from six to ten thus attached, and they appear to be grouped, furthermore, somewhat in couples like the so-called "diplococci." The individual cocci are small globular cells from 0.3μ to 0.4μ in diameter. They grow at ordinary house-temperatures, but more actively at a temperature of from 30° to 37° C. They are not particularly sensitive to the absence of oxygen, but grow best upon the surface of nutrient media. They are easily colored by the different aniline dyes, and are adapted to the Gram method of double staining.

In culture-media the cocci grow slowly (Fig. 9); in gelatin cultures the small white colonies appear throughout the whole length of the puncture. As a rule, there is not much growth on the surface, the growth reaching nearly its full development in four or five days. On agar the growth shows a similar tendency to collect in minute globular drops, which finally form a border at the margin of the scratch. The color of the points is white, and the growth at first has quite a transparent look, but later the centre of the colony has a faintly brownish color.

If it is desirable to obtain a considerable number of these cocci, they can be grown very rapidly in bouillon. The streptococci are found, in the normal state, in the saliva, in the secretion from the nostrils, in vaginal mucus, and also in the urethra. They are also found wherever the normal condition is disturbed by other diseases. We are apt to get what is called a "mixed infection" with this organism in typhoid fever, diphtheria, pneumonia, tuberculosis, scarlet fever, etc., and it is therefore probably an important agent in producing complications of those diseases.

Bacillus pyocyaneus is an organism found in green or blue pus. It occurs, however, only in open wounds, and is not, strictly speaking, a pyogenic organism, not usually producing suppuration. It is sometimes found in the serous secretions of wounds and in the perspiration. It is a small, thin rod with distinctly rounded ends, and may occur in chains of five or six links. It has very active movements. Spores are not seen to form. It belongs to those organisms which can grow where there is a small amount of oxygen, and develops at ordinary house- and oven-temperatures. When grown in gelatin there develops a shallow bowl-like depression, on the border of which there forms a beautiful green fluorescent pigment (Fig. 10). The depression widens until it reaches the borders of the test-tube, and then the greater part of the bacterial growth sinks to the bottom in thick, shining bands. The gelatin above gradually clears itself, and over the surface is formed a delicate yellowish-green film. The whole culture has a distinctly greenish tint. The pigment is deposited from the bacteria when in contact with oxygen, and it is therefore found only on the exposed edges of dressings. The substance then formed has been named "pyocyanine." According to Fränkel, if 1 c.cm of a fresh bouillon culture is injected into the subcutaneous tissue of guinea-pigs or of rabbits, a fatal infection is produced. By beginning with minimum doses only small abscesses will result, the animals finally becoming able to bear doses which would otherwise be fatal. Its prophylactic character was first discovered by Bou-

FIG. 10.—Bacillus Pyocyaneus.

chard, who showed that anthrax, even when already developed in the animal, could be cured by injection of this bacillus. Another variety, described by H. C. Ernst, is supposed by him to possess septic qualities, and still another is mentioned by Paul Ernst which is non-pathogenic.

Bacillus pyogenes fœtidus is found, according to Passet, in the pus of perirectal abscesses. It forms on the surface of gelatin a delicate white or grayish growth. On agar and on potato it has a light-brown color and emits an offensive odor.

Micrococcus tetragenus was first found by Koch in the tuberculous cavity of a lung, and is occasionally seen in morbid and healthy expectorations. It was found by Steinhaus in an acute abscess near the angle of the jaw: under the microscope the characteristic groups of four were observed enclosed in a capsule, and in very large numbers. It was also seen by Iakowski in two cases of acute abscess, one on the finger and the other in the palm of the hand. In culture-media the cocci do not grow in any special order, but in the tissues they are arranged in groups of four imbedded in a gelatinous membrane. The organism is aërobic. It colors well with all the aniline dyes and by the Gram method. On gelatin it appears as thick, globular, whitish masses with a somewhat glistening surface.

Bacillus coli communis (Escherich) was first discovered in 1885, at which time this micro-organism was reported as being constantly found in the discharges of cholera patients at Naples. Since then it has been found usually present in the normal dejecta. It is also found outside the body, both in air and in water and in putrefying fluids. Its presence in diarrhœal discharges and its near relation to the typhoid bacillus caused it to be studied very closely in order to find some method by which the two organisms could be separated. Lately the importance of this bacillus as a pyogenic organism and as a cause of septic and suppurative processes has been fully recognized.

The bacillus varies in shape with the media in which it is grown, and to some extent also with the source from which it comes. It is usually seen as a short rod, from 2 to 3μ in length and from 0.4 to 0.6μ in breadth, with rounded ends. It may grow in chains of from four to six filaments, though it is most frequently combined in pairs (Fig. 11). Sometimes these various forms are associated together, giving the microscopic field the appearance of a mixed culture. Spores have not been demonstrated, but the organism possesses very numerous and peculiarly arranged cilia. It stains readily with any of the watery or alcoholic solutions of the aniline dyes, but gives up its stain in the presence of iodine, and hence is decolorized by the Gram method.

The products of its growth are acid, as shown by the addition of litmus to the culture-media in which it develops. It grows freely on both acid and alkaline media with or without the presence of oxygen. It does not liquefy gelatin. On plates the colonies may have two distinct forms—one an irregular film, rapidly spreading over the surface with a slight opalescent appearance, and the other an ivory-white, heaped-up colony, which has no tendency to spread. In gelatin-tubes the bacilli grow along the whole length of the needle track and spread out on the surface of the gelatin. Sometimes a moss-like growth takes place into the gelatin from the needle track.

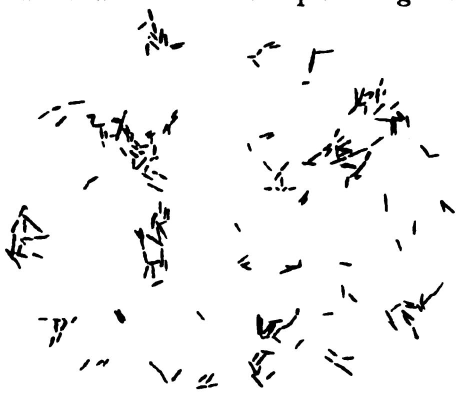
FIG. 11.—Bacillus Coli Communis.

The bacillus coli communis is distinguished from the typhoid bacillus by the fact that the latter does not form acid products in its growth and has no power to decompose grape-sugar or glucose, while the bacillus coli communis rapidly turns blue litmus red, and decomposes sugar, with the evolution of a considerable amount of gas. A large number of bacilli resembling this organism have been found by Jeffries, Booker, and others in the intestines, both in health and in disease. The rôle of greatest importance to the surgeon is played by this organism in the production of suppurative processes in the peritoneal cavity.

Fränkel found it under these conditions more frequently than any other organism, and in the majority of cases it appeared as a pure culture. Livy found pure cultures in the peritoneal fluid and in the secondary broncho-pneumonia of two patients who had died from strangulated hernia. He also obtained a pure culture from a case of abscess of the liver and from a lymphangitis of the arm. Richardson found pure cultures in fulminating appendicitis with perforation of the appendix. The bacillus has been found also in an anal abscess and in the urine of cases of cystitis.

Bartacci in a recent article shows that in nearly all the cases of

4

perforating peritonitis in man and in experimentally produced perforation in animals the bacillus coli communis is the only organism to be obtained by culture. Quite a number of other forms of bacteria exist in the extravasated fluids, but they do not appear to be able to grow in the presence of the bacillus in the ordinary culture-media. Bartacci does not, however, assume that the bacillus coli communis is therefore alone the cause of the septic peritonitis, but he thinks it proper to attribute part of the septic poisoning to the intestinal gases and fæces and to the various bacteria which they contain.

Experiments upon animals show that the effect produced by inoculation depends upon the source from which the bacilli are obtained. If taken from the normal intestine, they have no effect upon rabbits nor upon guinea-pigs. If the cultures are obtained where diarrhœa or ulceration is found, then the bouillon culture introduced into the peritoneum produces septic peritonitis or, in smaller doses beneath the skin, suppuration. Cultures which were violently septic have been found, on exposure, to become pyogenic. When, therefore, the soil on which it grows is modified by an intestinal lesion, this organism assumes a virulent condition, and if it can make its way into the peritoneal cavity or into any organ of the body, it is capable of setting up septic or suppurative processes of a greater or lesser degree of intensity.

Under favorable conditions other organisms may assume pyogenic qualities, such as the typhoid bacillus and the pneumococcus.

The *gonococcus* was first discovered in 1879 by Neisser, and subsequent investigation has sustained the conclusion that it is the specific organism which produces gonorrhœa. It is a comparatively large micrococcus, measuring 1.25μ in diameter, and is usually arranged as a diplococcus.

One of the most striking peculiarities of the gonococci, however, is the fact that they are accustomed to penetrate the protoplasm of, and to multiply rapidly in, the pus-cells. The nucleus of the cells is not touched by them. This characteristic grouping distinguishes them from nearly all other forms of micrococci. It is indeed very rare to see any gonococci outside the pus-cells. A cell may be so filled with them as to lose all its characteristic structure and appear only as a clump of cocci. The relation of the bacteria to the pus-corpuscles is regarded by some as evidence of its activity, by others as an illustration of the protective action of the phagocytes.

The gonococci are stained well with methyl-blue. They do not adapt themselves to the Gram method, as the iodide of potassium deprives them of their color. Neisser recommends the following method: A cover-glass having been prepared with a layer of the fluid to be examined in the usual way, it is treated for a few minutes with a concentrated alcoholic solution of eosin, the action of which is reinforced by heat. The excess of eosin being removed by blotting-paper, a concentrated alcoholic solution of methyl-blue is next applied for fifteen seconds, and then washed off with distilled water. The cocci are now seen colored blue, while the protoplasm of the leucocytes is stained a delicate pink and their nuclei blue (Fig. 12).

The gonococci do not grow on any of the ordinary culture-media, such as gelatin or agar or potatoes. Even on the media on which they do develop they are so frequently mixed up with other forms that the latter grow rapidly and present appearances which make it difficult to distinguish them from the genuine gonococci.

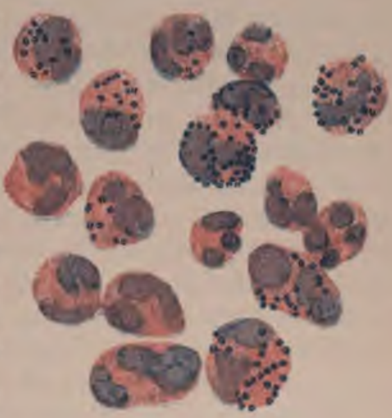
FIG. 12.—Gonococci.

Bumm has succeeded, however, in making them grow on human blood-serum, but this growth is accomplished with considerable difficulty. The materials used must, in the first place, be as free as possible from other organisms, otherwise the latter will outgrow the coccus. The gonorrheal pus, containing the organism in large numbers, must be placed on the surface of the blood-serum in drops of considerable size. Scratch- or stab-cultures are of no value. The test-tube must be placed in an oven at a temperature of from 33° to 37° C. The growth forms a delicate film with well-defined, irregular borders. It appears like a layer of varnish upon the top of the serum. When somewhat thicker it has a grayish-white or a slightly brownish tinge. The growth is slow and scant in amount. At the end of two or three days the cocci begin to die off, and the culture must therefore be often transplanted if it is desired to preserve the organisms. As nothing further will be said about this disease, it may be well to study here the action of the gonococci in the human epithelium.

For some time it was thought that sufficient proof had not been afforded of the specific character of the gonococcus. There is no one single characteristic which distinguishes this organism from all others, but the combination of peculiarities which have just been mentioned is such as is not found in other forms of bacteria. These peculiarities are—the diplococcus or "breakfast-roll" shape, the characteristic arrangement of the organism in the pus-cells, the bleaching caused by Gram's solution of iodide of potassium, and the difficulty of cultivation on ordinary media.

Proof positive has been afforded, however, by several experimenters of its contagious character. Bumm transplanted the twentieth generation of a gonococcus culture to the urethra of a bedridden paralytic, and produced a typical gonorrhœa. This experiment has recently been made upon the healthy urethræ of medical students. Bumm also examined the different stages of the gonorrhœal inflammation in the conjunctiva of new-born infants. Twenty-six fragments were taken from the conjunctival membrane at periods of the disease varying from thirty-six hours to thirty-two days. He found that the cocci, once having entered the conjunctival sac, reproduce themselves rapidly in the secretions, next invade the epithelial layer, and finally force their way down to the papillary layer. On the second day an enormous immigration of leucocytes takes place into the invaded layer of epithelium and the surrounding cells, pushing the epithelial cells, so as to lift them from their bed. On the papillary layer thus exposed there forms an exudation of a fibro-cellular character in which are clumps and rows of growing cocci. The bacterial growth does not invade the deeper tissue; it does not go beyond the most superficial of the sub-epithelial layers. A regeneration of the epithelium soon covers over the denuded spots, and the cocci, after growing for some time longer on the surface, gradually disappear. It is only on certain types of mucous membrane that these organisms will grow—namely, those which possess a cylinder epithelium or one closely allied to it. These are the membranes of the male and female urethra, the uterus, Bartholin's glands, and the conjunctiva. The more deep-seated secondary inflammations, such as involve the prostate, the epididymis, the testicles, the uterus, and the tubes, are frequently due to the presence of some of the pyogenic bacteria; but suppurative inflammation of both tubes and ovaries has been found to be due largely to the presence of the gonococcus. The aureus has been found as a frequent companion of the gonococcus in the urethral discharge and in the pus from gonorrhœal buboes. The metastatic inflammation of joints and the endocarditis which occur as sequelæ of gonorrhœa have been supposed to be due to the presence of pyogenic cocci, but Councilman and others have shown that the gonococcus may be the sole organism concerned in the inflammatory process.

Why the gonococcus should grow only in the superficial layers of certain mucous membranes, and nowhere else in the body, has not yet been satisfactorily explained. The most plausible theory seems to be that inasmuch as the gonococci possess a very marked preference for oxygen, they find a better culture-soil in the epithelium than in the subjacent connective tissue. Bumm has shown that injections of pure gonorrhœal discharge or of pure cultures of the gonococcus into the subcutaneous tissue do not produce suppuration. That this loss of activity is not explained by the action of phagocytes is shown by the fact that the organisms, when the tissues are examined later, are not taken up by the cells of the part, but are nearly all to be found outside the leucocytes.

After the gonococci have existed for a certain length of time in the epithelium of the part, they disappear spontaneously in a certain number of cases. This disappearance is accounted for by the casting off of the cylinder epithelium during the inflammatory processes, and its replacement by a pavement epithelium which resists the efforts of the cocci to penetrate it. In this way proper nutriment gradually fails them and they die out. It is generally accepted that cure is effected in this way rather than by the phagocytes, for such leucocytes as are invaded by the gonococci are destroyed by the latter during the active growth and multiplication of the organisms which take place in the protoplasm of those cells.

Streptococcus erysipelatis in all respects so closely resembles the streptococcus pyogenes that the majority of bacteriologists are unable to detect any constant differences between them either by the microscope or by culture. The description of the organism coincides with that already given to the streptococcus: therefore it is needless to repeat it here. Rosenbach undertakes to recognize certain distinguishing marks between the two. He thinks the cocci and the chains of the erysipelas coccus are larger than those of the pyogenic coccus. His delineations of the culture show a growth of the erysipelas coccus more transparent and more irregular and nodular in outline than is seen in the cultures of the other organisms. The brownish tint of the culture is also wanting. The weight of evidence at the present time is, however, in favor of the identity of the two organisms. The question is discussed more at length in the chapter on Erysipelas.

Bacillus Tetani.—The first observations on the nature and origin of this organism were made in 1884 by Nicolaier, who found a bacillus in garden soil, and who succeeded in producing tetanus in mice, guinea-pigs, and rabbits by injecting the soil into them subcutaneously. The same organisms were found in the diseased animals, but there was great difficulty in obtaining a pure culture of the bacilli, thus giving conclusive evidence of its power to produce the disease. This culture was finally accomplished in 1889 by Kitasato, who planted on a suitable culture-soil a fragment of tissue from the neighborhood of a wound in a man dead of the disease. He found that the spores of this bacillus germinated before those of the other forms of bacilli mixed with it. As soon as these spores had formed he subjected the culture to a temperature of 80° C., which killed off all bacteria; consequently, the spores of the tetanus bacillus alone, remained, and a pure culture of this organism was obtained as soon as the bacilli had developed from them. The spores are found in garden soil, in masonry, in decomposing liquids, and in manure.

The tetanus bacillus is a large slender rod with somewhat rounded ends. It resembles the bacillus of mouse septicæmia, but

FIG. 13.—Bacillus Tetani.

is longer: in fact, it sometimes grows into long chains which show very imperfectly the lines of division. The spore-formation takes place at the end of the bacillus, and, as it enlarges the cell considerably, gives it a "pin" or "drumstick" shape (Fig. 13). The spore germinates at a temperature of 37.5° C. in thirty hours; in the temperature of a house, in about a week. It is motile, and belongs to the strictly anaërobic organisms, rapidly dying when exposed to the air. It is readily colored by methyl-blue and fuchsin, and is brought out very perfectly by the Gram method. It can be cultivated in gelatin mixed with grape-sugar, which aids in its rapid development. The upper portions of the gelatin remain sterile, but in the lower portions of the puncture there is an active bacterial growth which sends out innumerable little prolongations, giving to the culture the appearance of an inverted fir tree. After the first week the gelatin begins to liquefy and to obscure the peculiar features of the growth, until, finally, the gelatin is changed into a whitish-gray, tenacious, shining mass.

To obtain cultures of the tetanus bacillus from cases of traumatic tetanus in man or from experiment animals the following method may be employed, which is a modification by Frothingham of Kitasato's method :

Inoculate tubes of decidedly alkaline bouillon with pus from the wound or point of inoculation. If there is no pus, small fragments of tissue are snipped from the region of the wound and used for this purpose. The tubes should now be placed in an atmosphere of hydrogen at a temperature of from 37° to 39° C. At the end of forty eight hours a microscopic examination may be made, and if the tetanus bacilli are found, the tubes are to be heated for three-quarters of an hour to one hour in a water-bath previously heated to 80° C. From these heated tubes fresh alkaline bouillon may be inoculated.

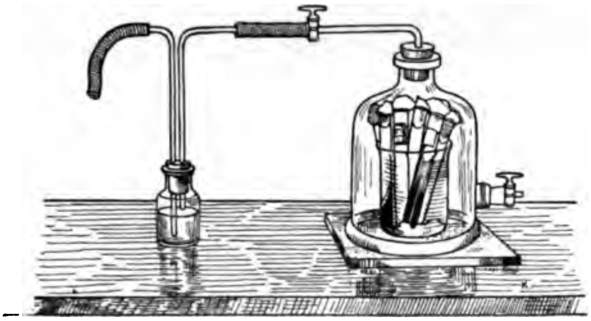

FIG. 14.—Hydrogen Jar for Anaërobic Cultures. The stop-cock on the right allows the air to escape from the jar, while the hydrogen is passed in from the left.

These fresh cultures may be allowed to develop under hydrogen at a temperature of 37° C. for forty eight hours (Fig 14). Pure cultures should be obtained in this way, the purity of the culture being verified by microscopic examination and growth on solid culture-media, and the virulence being determined by inoculation experiments.

Brieger has obtained from cultures a toxine which he named "tetanin," and in addition "tetanotoxin" and "spasmotoxin," all of which, when injected into animals, produce convulsive movements and, finally, paralysis. Inasmuch as the same group of symptoms were obtained by the toxines as were obtained by the bacilli, and as the latter are hard to find in the blood and internal organs of individuals affected with tetanus, it has been thought probable that the symptoms of the disease are largely produced by these chemical substances.

Although Rosenbach and Shakspeare have stated that the bacilli are to be seen in the central nervous system, subsequent observers have not been able to find them, and it is probable, therefore, that the convulsions are produced by the tetanin elaborated by these organisms.

Bacillus Tuberculosis.—Although experiments were made as early as 1865 by Villemin to prove the inoculability of tubercle, and as Cohnheim in the following decade decided that tuberculosis was a specific infectious disease, it was not until 1882 that Baumgarten and Koch simultaneously discovered the organism which causes the disease. Baumgarten should receive credit for first having seen the bacillus with the microscope, but it remained for Koch to cultivate it successfully and by inoculation to prove beyond question its right to be considered the cause and only cause of tuberculosis.

The tubercle bacilli are small and thin rods about 2 to 4μ in length; that is, about one-quarter to three-quarters the length of the diameter of a red blood-corpuscle. The ends of the rods are generally slightly rounded, and are usually slightly bent near the middle or are more or less curved. In artificial cultures the rods are a little smaller than when growing in the tissues. The longest rods are usually seen in phthisical sputa. They are generally single, occasionally being found in pairs arranged like a V, and sometimes several are strung together. They do not possess the power of motion. Whether spore-formation takes place is undetermined, although Baumgarten thinks it highly probable that it does occur, as a cheesy material, in which it is impossible to demonstrate the bacilli by any method of staining, when inoculated into animals produces the disease. Free spores have never been seen, nor have the bacilli been observed in the act of spore-formation. In the fresh state none of those bright, glistening spots are seen which are characteristic of spores. When colored, the bacilli exhibit, placed in regular order, bright spots which are very suggestive of spores. The expectorations can be kept months, and even years, in a dried state without destroying the vitality of the bacilli. The acids of the stomach and the products of decomposition have no effect upon them. Pure cultures of bacilli have been mixed with the food of animals, and have thus been passed through the digestive tract without any effect upon their vitality. This durability seems to be due to the unusually tough cell-wall which the bacillus possesses. The organism is a facultative anaërobic; that is, it may grow without oxygen, although it prefers to grow with oxygen.

This is one of the few bacteria which have a pathognomonic stain. Though taking the ordinary watery and alcoholic aniline stains with difficulty, yet when properly stained it does not give up its coloring material even in the presence of mineral acids—a property which the bacillus of leprosy alone holds in common with it.

The following is a convenient method (Ziehl) of examining the sputa:

The sputum selected is spread out upon a glass with a dark background to enable one to detect the various details, such as the fragments of the diseased lung, the secretions of the upper air-passages, and the saliva. The bacilli are usually found in the lung-fragments, which are small, tough, yellow clumps floating in the saliva. One of these clumps is removed by the sterilized platinum needle and placed upon a cover; a second cover-glass is then placed upon the first, and the specimen is gently pressed between the two so as to form a thin layer, whereupon the glasses are separated by a sliding motion and are allowed to dry in the air. To complete this process the glass to be stained is rapidly passed three times through a flame. A few drops of carbolic fuchsin [1] are allowed to trickle over the glass, and it is held over the flame until the coloring fluid partially evaporates. More staining fluid is now added, and the heating repeated until a satisfactory coloring is obtained, or the coloring fluid containing the specimen can be placed in a watch-glass and heated for a few moments over a water-bath. The specimen is then washed with distilled water. To decolorize the surrounding cells and other forms of bacteria a strong decolorizing agent must be used, as, for example, a 5 to 10 per cent. solution of sulphuric acid. The glass is moved up and down in this solution until the deep-red color becomes a yellowish brown. Next place the glass in 70 per cent. alcohol to wash out the dissolved fuchsin. Wash with distilled water and color again with ordinary watery solution of methyl-blue. Wash, finally, with distilled water and examine, wet or dry, the specimen, and mount it permanently in Canada balsam.

The specimen is examined to the best advantage when wet, as the bacilli are not so much shrivelled as when mounted in Canada balsam. The tubercle bacilli will be found colored red, and any other bacteria which happen to be present, and which have been deprived of their red color by the acid, are stained blue, so that the different kinds can thus readily be distinguished from one another (Figs. 15, 16). The method may be simplified by dipping

[1] Fuchsin 10 parts in 100 parts of a saturated aqueous solution of carbolic acid.

the red-colored specimens into a solution in which the acid and

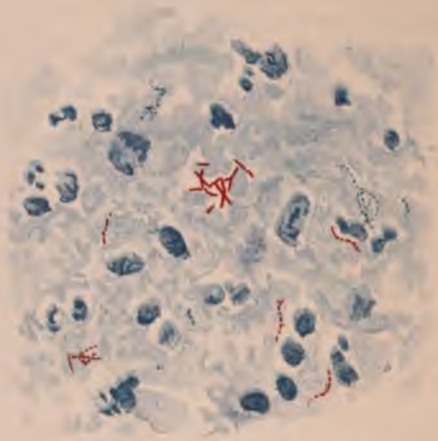

FIG. 15.—Tuberculous Sputum.

the methyl-blue are both present: water, 50 parts, alcohol 30 parts, nitric acid 20 parts, and methyl-blue to saturation. This

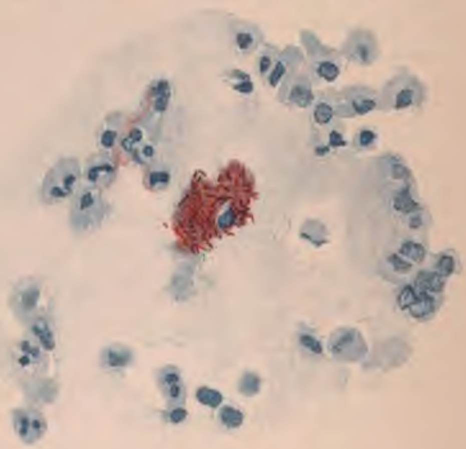

FIG. 16.—Tuberculous Urine.

simplifies the process somewhat. Sections are colored very much in the same way:

Place the section for half an hour in a dish of carbolic fuchsin ; allow it to float for one minute in a 5 per cent. solution of sulphuric acid ; wash in 60 per cent. alcohol. Next stain with methyl-blue for two or three minutes. Wash in water and weak alcohol, dehydrate in absolute alcohol, and, having cleared it in oil of cedar, mount in Canada balsam.

Although for clinical work the short methods may be used in the hands of experts, still it must be remembered that the Ziehl solution stains a number of spores, which, unless recognized, may prove a source of error. It is not generally known that under certain conditions—for example, age—the bacilli may not be stained by the quick methods. When stained for twenty-four hours according to the now nearly-forgotten Koch-Ehrlich method the bacilli are well defined. For this reason the Koch-Ehrlich method is given. It should however, be remembered that this method shows crystalline forms which may be mistaken for bacilli:

Place the section in aniline-water fuchsin for twenty-four hours; decolorize in a 25 per cent. solution of nitric acid; wash in 60 per cent. alcohol; place in watery methyl-blue for a few moments; wash and mount.

Under the microscope is seen the miliary tubercle consisting of leucocytes and epithelial cells, and a giant-cell in or near the centre of the growth. The bacilli are found lying in small numbers between the leucocytes and in the giant-cell. The nuclei of the giant-cell appear to be arranged in a radiating manner at its periphery, as do also the bacilli. This arrangement is due to the fact that the centre of the cell has undergone degeneration and its contents at this part have disappeared. This appearance is quite characteristic of the tubercular giant-cell, and distinguishes it from the giant-cell of sarcoma (Fig. 76). The degenerative process is seen also in the other cells at the centre of the tubercle, while new cells and bacilli are seen on the borders. In this way the growing tubercle undergoes a cheesy degeneration at its centre. If the disease at this stage is on the surface of the skin or a membrane, ulceration will occur.

The growth of the organisms is exceedingly slow, and takes place at the temperature of the human body, and very slight deviations from this point are likely to arrest their development.

Koch devised expressly for this organism the hardened blood-serum. Nocard and Roux have suggested a combination of agar with glycerin, upon which it grows even better, as the bacillus seems to have a predilection for glycerin, and this being also much more easily sterilized. When cultivated in the test-tube on agar thus prepared, a well-developed growth is procured at the end of fourteen days, while on blood-serum from one to two weeks more must pass before the culture reaches the same point. It then appears as thick crusts of a dull grayish-white color, which crusts are very dry and brittle and are made up of minute scale-like masses (Fig. 17). If the growth meets a drop of condensed moisture, it will form a thin film over the latter, without in the least disturbing the clearness of the fluid.

FIG. 17.—Bacillus of Tuberculosis on glycerin-agar.

To obtain materials with which to make a series of pure cultures tuberculous sputa may be injected into a guinea-pig. When tuberculosis is established, the animal should be killed, and a fragment of tubercle taken, with due precautions, from the lung and placed upon the culture-soil. After development takes place the fragment of lung can be seen under a low power, and surrounding it are seen S-shaped, wavy, and scroll-like masses of bacilli.

The tubercle bacillus is not found growing outside the living tissues of man and animals, the necessary conditions of nutrition and temperature not existing elsewhere. They must be regarded, therefore, as true parasitic organisms. Although they are unable to grow around us, their great power of resistance permits of their being preserved for a long time in a dried state mixed with dust, and of taking on an active growth whenever an opportunity occurs for them to become grafted again upon the living tissues.

This inoculation may take place on the skin following slight blows or bruises or cuts. The hands of attendants on the sick may be cut with a glass containing sputa. Anatomical tubercle is an example of this form of contagion. The disease known as "lupus" is but a variety of tuberculosis of the skin. As has been seen, the bacillus is extremely resistant to the action of the digestive fluids, and animals experimentally fed with this organism have succumbed to a general tuberculosis. Whether inoculation can take place through the uninjured mucous membrane has not been demonstrated, but it is probable that if bacteria can penetrate the uninjured skin, they can also work their way through a normal mucous membrane. As a rule, the mesenteric glands are found first affected, and afterward the mucous membrane—a sequence which is at least suggestive that the membrane was previously in a healthy condition. Later, the spleen and liver are found infected. A very practical deduction from these experiments is the necessity for the supervision of food, particularly the milk of tuberculous cows. It is now well known that the organisms are found in the milk. H. C. Ernst has shown that six drops of infected milk injected subcutaneously into a guinea-pig will produce a general tuberculosis even though there be no manifestations of disease in the udder.

The question of an infection through the respiratory tract appears to be a disputed one. According to Baumgarten, experimental work seems to point against such mode of entrance into the system. Fränkel, who writes with the authority of Koch behind him, takes the opposite view, and believes that breathing infected air is the most frequent mode of acquiring the disease. Experiment shows that the disease appears first at the point of infection, and therefore is at first local. The frequency of the disease in the lungs surely points strongly to the respiratory tract as the route through which infection takes place. Inasmuch as it has been proved that bacilli can float in the air when dry, it is probable that they are in this way conveyed from one individual to another. The durability of the organism, as already seen, protects it from the injurious influences of desiccation. As Stone has shown, it may retain its vitality in this condition for three years. How this transfer may take place has been explained by the investigations of Cornet. He demonstrated that the organisms are not found distributed indiscriminately in the air and other surroundings, but that they are found only in localities frequented by tuberculous patients, in such places as one would expect to find their expectorations. This he demonstrated by injecting the dust of infected localities into guinea-pigs, thus producing the disease. The dust of other localities produced negative results. The bacilli are therefore frequently found in houses inhabited by tuberculous individuals. The organisms, having been expectorated on the floor or on handkerchiefs, are subsequently disseminated through the building in the form of dust. Cornet regards with suspicion hotels or hospitals occupied by consumptives, and the same may be said of factories, prisons, or other buildings where large numbers of individuals are congregated. Cornet strongly advises that tuberculous sputa should not be allowed to dry up, but should be kept in a moist state.

Bacillus mallei (bacillus of glanders; rotz bacillus; morve).—This organism was discovered by Löffler and Schütz, who made their announcement in 1882. They demonstrated the presence of the bacilli in the diseased tissues, cultivated them outside the living organism, and inoculated them successfully into animals, thus reproducing the disease. These organisms are somewhat shorter than, and not quite so thin as, the tubercle bacilli; that is, in length they are about two-thirds the diameter of a red blood-corpuscle. They are frequently arranged in couples, side by side, but generally are single. In culture several of them may be linked together in a chain (Fig 18); in the tissues they are distributed in clusters, either parallel with one another or pointing in various directions. They possess no movements of their own. The pres-

FIG. 18.—Bacillus Mallei.

ence of spores has been doubted, and the peculiar bright spots seen when the bacilli are colored are not spores, but are evidences rather of a degenerative change. Baumgarten has, however, by a special method of staining, been able to show that in some cases at least they are able to form spores. He does not think, however, the spore-formation takes place in the living tissue. The durability of the glanders bacilli is not, however, apparently great; they do not bear desiccation more than two or three weeks; exceptionally they may last as long as three months. The so-called "spontaneous glanders" which occurs at long intervals after the existence of a local epidemic may be explained possibly by the presence of spores. They belong to the facultative-anaërobic bacteria, and grow best at a temperature of from 30° to 40° C. They belong to that class of bacteria which takes the staining fluid easily, but they as readily lose their color. One of the simplest methods of staining is to treat a cover-glass preparation with warm carbolic fuchsin, and to wash off with a 2 per cent. solution of nitric acid. No method of double staining has yet been successful. In staining sections they should be placed six to eight hours in carbolic methyl-blue, then in acetic-acid solution, and finally in distilled water. Having been dried on the object-glass with a current of air, they are cleaned in xylol and mounted in Canada balsam.

The bacilli can be grown upon a 4 per cent. glycerin-agar. When cultivated upon this soil, hardened obliquely in a test-tube at a temperature of 37° C., they form on the fourth or fifth day a white, transparent, moist, glistening film along the needle track. The growth on potato is very characteristic, it forming here a yellow, transparent, honey-like layer which appears on the second day. In a few days it becomes deepened in hue and less transparent. For a short distance around the border of the culture the potato acquires a yellowish-green color. No other organism presents these appearances under cultivation. When seen in sections under the microscope, the bacilli are found singly or in small groups, the latter evidently having developed in a cell which has subsequently broken up. The capillary vessels do not seem to be involved, a fact which corresponds with their rare occurrence in the circulation. The greatest collection of bacilli is in the centre of the nodule or tubercle—a condition which is almost as characteristic of glanders as it is of tuberculosis. As the border is approached few organisms are found. The majority of the bacilli lie between the cells. The principal cells of the nodule are the epithelioid cells; giant-cells are never seen. As the nodule develops leucocytes abound. The pathological changes which follow resemble the softening of suppuration. The process seems to stand midway between the cheesy degeneration of tubercle and the suppuration produced by the pyogenic cocci. Very few of the organisms are found in the secretions from the nostrils. It has been found that the bacilli readily lose their virulence after several generations of culture have been reached, and this points to the fact that, outside the living organisms, the conditions are unfavorable for their preservation. The bacillus mallei probably does not grow out of the living tissues except under very favorable circumstances, it being for the most part a true parasite.

The virus can readily be inoculated into horses, and the disease with all its characteristic symptoms may thus be reproduced. Asses are also susceptible to glanders, as are goats, cats, field-mice, and guinea-pigs. Pigs, white mice and house-mice, and oxen, however, possess a certain immunity. Lions and tigers have succumbed to the disease by infection experimentally produced by mixing the virus with their food. The virus acts first at the point of inoculation, and thence spreads slowly throughout the tissues, the blood remaining almost entirely free from bacilli. At the post-mortem examination nodules are found in the spleen, the liver, or the lungs.

In examining a glanders nodule which has not yet broken down one is generally able to discover the bacilli in colored sections; but it is well at the same time to make a potato-culture, which will, if the bacilli are present, show the characteristic growths.

If it is desired to examine the nasal secretions or discharges from ulcers, a satisfactory result will not be obtained by the above methods, for here the bacilli are not numerous, and are mingled with different kinds of bacteria which resemble them. This difficulty is overcome by inoculating guinea-pigs with the material to be tested. Field-mice, which are otherwise suitable for inoculation, are liable to die of septicæmia. If the bacillus mallei be present, it will be found in the nodules that develop with the disease.

Bacillus of Leprosy.—A few words on this organism are appropriate in this chapter, as leprosy is a disease closely allied to tuberculosis, and its organism bears points of resemblance both to the tubercle and to the glanders bacillus. The disease is one which also occasionally comes to the surgeon for operation. This bacillus was first described in 1880 by Hansen, whose work was later continued by Neisser, a skilled bacteriologist. The bacilli of leprosy in appearance are almost exactly like the tubercle bacilli. They are long and slender rods with somewhat sharpened ends, and are, like the tubercle bacilli, without power of motion. It is doubtful also whether the clear uncolored portions seen in the bacilli after staining are or are not spores. As has already been shown, they are the only organisms which react in the same way as do the tubercle bacilli to coloring reagents, which, however, they take somewhat more readily. The readiness with which the bacilli are stained by the ordinary aqueous and weak alcoholic solutions of the aniline colors and also by the Gram method serves to distinguish them from the tubercle bacilli.

Although the bacillus of leprosy is found in all cases of the disease, it is not fully identified as the *cause* of the disease, it being impossible to obtain reliable cultures by any of the known methods. Inoculations by Bordoni of animals with the bacillus have been, without exceptions, failures, which Bordoni explains by the rapid weakening of the bacillus when removed from the body. Melcher and Ortmann placed fragments of nodules from a patient immediately in the anterior chamber of the eye of a rabbit, and observed the animal die of the disease several months later. At the autopsy small nodules were found in the internal organs, and the presence of the bacilli was demonstrated in them. Arning inoculated a condemned criminal in the Sandwich Islands with material cut from a leper. Some months later a nodule appeared at the point of inoculation, and at the end of five years his death took place, general leprosy having developed.

The bacilli are ordinarily found in the skin and the tissue surrounding the nerves, and in the lymphatic glands, the spleen, and the liver, but they are rarely found in the blood. Their tendency is to grow in clusters, appearing usually inside of cells, some of which are epithelioid in character, and others apparently are leucocytes. These cells have been called "lepra-cells" by the Germans, but some observers denied the existence of such cells, and claimed they were merely clusters of bacilli lodged in dilated lymphatic vessels. Such clusters form a characteristic appearance in discharges from lepra sores.

Syphilis Bacillus.—The question of the microbic origin of syphilis has been extensively discussed and investigated, but as yet no definite conclusions have been reached which are generally accepted by bacteriologists.

The most important contribution to this study was made by Lustgarten, who in 1884 announced that he had discovered in the tissues and in the discharges from syphilitic ulcers a bacillus closely resembling the tubercle bacillus, but distinguished from other forms by its peculiar method of staining. The bacillus of syphilis usually is slightly curved or S-shaped.

To color it a section should be placed for from twelve to twenty-four hours (at the ordinary room-temperature) in a solution of aniline-gentian-violet, and for two hours be kept at a temperature of 40° C., and then placed in absolute alcohol for a few minutes; next placed for ten seconds in a 1 per cent. watery solution of permanganate of potash, then for a moment in a strong watery solution of sulphuric acid, and finally washed out in distilled water. If sufficiently decolorized, it may then be mounted in the usual way. The same method may be used for the cover-glass preparation, except that water should be used instead of the absolute alcohol after staining, and the other steps of the process should follow one another more rapidly.

A simpler method is to keep the cover-glass in a hot solution of fuchsin for a few minutes, leaving sections for twenty-four hours in a cool solution, and then bleached in at first a weak and afterward in a concentrated solution of chloride of iron. Cover-glasses are washed in water and the sections in alcohol.

The bacilli of syphilis are found always enclosed within large cells. Lustgarten maintains that he has found these organisms in all cases of syphilis examined by him, but those who have carried out his methods have been unable to find them. They have been seen oftener in the cover-glass preparations than in the sections. Glanders and tubercle bacilli are stained also by Lustgarten's method, but his syphilis bacilli appear to lose their color more easily. Lustgarten's attempts to cultivate these bacilli were not successful. They are said to have been grown upon a gelatin prepared from the bladder of Russian sturgeon. Transplantation of a fragment of tissue on gelatin left at the ordinary house-temperature produced a grayish-yellow growth around the fragment at the end of thirty-seven days. Inoculation was made also with the blood of an infected monkey, and the brownish growth produced was seen, on examination, to be composed of small bacilli. Granules were found also in the cultures which were thought to be spores.

In 1885 a discovery was made which threw a great deal of doubt upon the genuine nature of the syphilis bacillus. Two observers simultaneously demonstrated a bacillus in the preputial and vulvar smegma bearing a striking resemblance to Lustgarten's bacillus. Its appearance and reaction to staining were the same. The smegma bacilli were supposed to lose color a little more rapidly than the other form, but this difference does not appear to be constant. The only variation between the two forms is that, while both could be found in discharges from the vulvar or the preputial sores, or, possibly, also elsewhere in ulcerations of the surface of the body, the smegma bacilli could not be found imbedded in the tissues. Many authorities of note are inclined to think that some relation exists between these organisms and syphilis.

But this is not the only organism which has been reported as the cause of the disease. Eve and Lingard described a bacillus cultivated from the blood and the diseased tissues in syphilis. It resembles the tubercle bacillus, but it is stained by the ordinary aniline dyes and by the Gram method, Lustgarten's method yielding negative results. A pure culture was obtained by inoculating hardened blood-serum with the blood or weak fragments of tissues from syphilitic patients. The growth appeared as a thin, light-yellow or greenish layer. Inoculation of monkeys from this culture were not successful.

Disse and Taguchi examined the blood of patients with secondary syphilis, and they almost constantly found cocci 1μ in diameter, isolated or in colonies, between the corpuscles. The cultures upon the different media appeared as grayish-white masses, and all culture-media except serum were liquefied by them. This is, according to some, the only organism which liquefies agar-agar. Gram's method of staining yielded good results. The most important claim of these organisms to be regarded as the cause of syphilis was the inoculation of rabbits, dogs, and sheep, and the production of a chronic infectious disease which was transmitted to embryos developed before and after the inoculation.

Inoculation of animals with the discharges of the diseased tissue of syphilitic patients has not always been attended with positive results. Kelbs successfully inoculated monkeys with the liquid obtained from an excised chancre, in which liquid he had found bacilli. He made a culture in liquid gelatin and inoculated the culture-fluid. Buccal ulcerations developed in appearance somewhat like *plaques muqueses*. Caseous deposits resembling gummata were found in the dura mater. He also implanted a fragment of a chancre beneath the skin, and obtained caseous deposits, which, however, resembled tubercle.

Martineau and Hammic placed in culture-bouillon fragments of chancres, and subsequently found a growth of bacilli. They obtained, by inoculating monkeys with this fluid, eruptions resembling those of syphilis. An inoculation of the prepuce in three places was followed, twenty-eight days afterward, by the development of nodules which resembled indurated chancres. Secondary symptoms were also developed.

Although no satisfactory demonstration has been made, it seems highly probable that syphilis is of bacterial origin and that the organism is a bacillus; but the necessary identification by culture and inoculation has not yet fully been worked out.

Bacillus of Malignant Œdema.—This organism was first described by Pasteur as the *vibrion septique*, under which name it is to be found in French works on bacteriology. Its present name was given it by Koch, and it is an organism found in one of the laboratory diseases of animals. It is occasionally also found in the traumatic gangrene of man, and therefore deserves a place here. It has often been mistaken for the anthrax bacillus, but from which it is now readily distinguished. It is evidently a saprophytic organism, and is found in decomposing substances, in dirty water, and in dust, but is chiefly found in rich garden-mould. If such soil is injected into a guinea-pig, the animal dies in twenty-four or forty-eight hours, the œdema bacilli being found as the cause of death. They are slender rods, considerably narrower than anthrax bacilli, and are frequently seen together in bands which are often bent and curved. The bacilli have an active motion, but this motion soon ceases when the organism comes in contact with oxygen. Spores are formed in a temperature of above 20° C. They are large and are situated at the centre or the end of the rod (Fig. 19), which appears slightly distended at this point. The

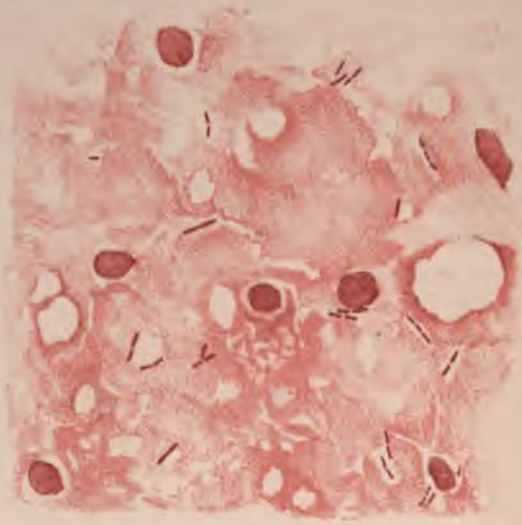

FIG. 19.—Bacillus of Malignant Œdema: cover-glass preparations from the liver of a mouse.

bacilli are strictly anaërobic, and are sensitive even to the slightest traces of oxygen. They take well the aniline staining-fluids, and when colored the pointed ends of the rods distinguish them from the anthrax bacilli. They do not stain well by the Gram method.

They grow best in gelatin cultures to which has been added from 1 per cent. to 2 per cent. of grape-sugar. In the early stages they form varicose prolongations at the lower portion of the needle track, and on the periphery form radiating fibres. Later the gelatin melts gradually into a cloudy, opaque mass. There is usually a gas-formation which distends the needle track nearly to the surface. The gas has a disagreeable odor, but it does not have the peculiar foul smell evolved by the genuine bacilli of putrefaction.

If a pure culture of the œdema bacillus is subcutaneously injected into a guinea-pig, there is obtained an extensive bloody, œdematous exudation of the muscular layer, but no pus nor foul odor and very slight gas-formation. The changes in the internal organs, liver and spleen, are very trivial. If, however, garden-soil is substituted for the pure culture, there is then obtained an infiltration of the same tissues, with a dirty reddish serum which has a foul odor, and which may be purulent and be accompanied with an abundant gas-formation—in short, the picture of a progressive gangrenous emphysema such as is often seen in traumatic gangrene in man. In this case there are found, in addition to the bacilli of œdema, other forms, such as the "pseudo-œdema bacilli," etc. A case of this kind is reported by Rosenbach—a compound fracture of the thigh and leg with subsequent gangrene. The thigh was amputated in the upper third. From the foul decomposing tissues of the limb a culture was taken immediately after the operation, from which culture he obtained a "saprogenic bacillus."

The internal organs are but slightly affected. If an animal be examined immediately after death, the œdema bacilli will be found in the superficial tissues of the body, but never in the blood-vessels. This arrangement is in striking contrast to that of the anthrax bacilli. But after death they rapidly spread throughout the body, and an active spore-formation occurs which does not take place during life. In the mouse inoculated with the bacilli of malignant œdema the course of events is somewhat different from that observed in the rabbit and guinea-pig: a rapid invasion of the entire body takes place during life, and the condition might easily be mistaken under these circumstances for anthrax. According to Chauveau, an animal which had recovered from malignant œdema was ever after insusceptible to this disease. Roux and Chamberlain report that they obtained from the culture of these bacilli soluble substances which, when injected into animals, protected them from the action of the bacilli themselves. The ptomaïne was obtained either by destroying the organisms with heat or by removing them with a filter, or the œdematous fluid from an inoculated animal was used. An immunity was thus obtained.

The "*pseudo-œdema*" *bacillus* is described by Flügge and Liborius, who found it a frequent companion of the œdema bacillus. The pseudo-œdema bacillus is a somewhat thicker rod than the bacillus of malignant œdema, and possesses a very bright border.

It is distinguished also by the formation of two spores in each rod. The bacilli are strictly anaërobic. In sugar-gelatin they are accompanied in their growth by an abundant gas-formation, which has an odor of old cheese. Small doses of the culture are not infectious; in large doses it kills mice and rabbits. Bordoni and Uffreduzzi in 1889 obtained from the cadaver of a man who had died of a disease similar to anthrax an organism closely resembling the pseudo-œdema bacillus, to which organism they gave the name "*proteus hominis.*" Tricomi, an Italian observer, found a slender, long bacillus in the blood of patients suffering from senile gangrene, and also around the line of demarcation and in the adjacent healthy tissues. He cultivated the organism on the various media, stained it with the aniline dyes, and succeeded in producing gangrene in animals at the point of inoculation of the pure culture.

Godwin obtained from a case of gangrenous emphysema cultures of streptococcus and the albus. W. Koch obtained from a case of progressive gangrene in a young man a bacillus closely resembling the bacillus of glanders. Bonnomé found the pyogenic cocci in a case of gangrene of the lung in man, and by mixing the cultures with fragments of pith, as has been shown elsewhere (p. 145), he enabled the cocci to be caught in the lungs of animals inoculated, thus reproducing the gangrene of the lung. Lingard found long bacilli in noma, and similar organisms in gangrenous stomatitis of cattle. Ranke found in cases of noma streptococci similar to those found by Koch in his experiments on field-mice.

As Senn justly remarks, there is no specific organism to blame for traumatic gangrene, which may be caused, he thinks, either by the mechanical obstruction of the vessels by large numbers of organisms in the capillaries, or by the chemical action of the ptomaïnes on the tissues, or, finally, by the excess of exudation in a part which mechanically obstructs the return of the venous blood.

Those appalling forms of traumatic gangrene, which are described elsewhere, are in many cases probably caused by the bacilli of the class to which belong the œdema and pseudo-œdema bacillus, which, with the pyogenic cocci, are always present, and are ready to attack wounds occurring in foul parts of the body or in tissues whose vitality has been destroyed by some injury.

Bacillus Anthracis.—This organism deserves a place among surgical bacteria, not only because it produces the malignant pustule in man, but also on account of its historical position among bacterial diseases. It was not only the first of bacteria found in diseased blood and tissues, but the investigation which demonstrated it as the true and only cause of splenic fever formed also the foundation upon which the science has subsequently been built up.

In 1850, Davaine and Rayer announced to the Académie des Sciences that in animals affected with anthrax there existed in the blood little filiform bodies about double the diameter of a red corpuscle in length. These bodies did not possess spontaneous movements. After the subject had begun to attract the attention of the scientific world it was more carefully studied by Davaine himself, and later by Pasteur. But it was due to Koch that the existence of spores was discovered, and that cultures of the bacilli could be made and injected into animals, thus reproducing the disease.

The bacilli, when grown on culture-media, are seen under the microscope as bright, transparent rods with slightly rounded ends. They are from 1 to 1.5μ in thickness and from 3 to 6μ long, and are entirely without the power of motion. If such bacilli are placed in bouillon and examined under the microscope, it is possible to observe the process of division, which takes place rapidly under somewhat high temperatures. The short rod-like cells grow to long staffs which stretch across the field of vision, and which show only here and there indications of being made up out of several cells. They now become somewhat less transparent, and, growing to great length, the chain of bacilli becomes twisted up into characteristic coils or knots (Fig. 20).

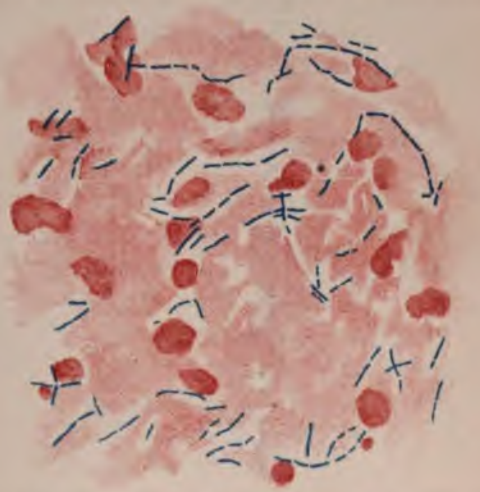

FIG. 20.—Bacillus Anthracis; cover-glass preparations from the liver of a mouse.

If, however, the bacteria are taken from the blood of an animal dead of anthrax, and are colored in the usual manner, there is no longer seen the rounded ends just alluded to. They now appear somewhat larger at each end than in the centre, and articulate, as it were, with the other rods of the chain, like the phalangeal bones or the joints of a bamboo rod. This appearance is best shown with Bismarck-brown or methyl-blue. These organisms, when in the tissues, can be demonstrated by Gram's method, but they have an altered and granular appearance. The articulating enlarged ends of the bacilli are peculiar to anthrax, and distinguish these bacteria from all other forms. In using Gram's method care must be taken not to bleach too much, as the bacilli readily give up their color.

If it is desired to see the spores, the bacilli must be examined in a drop of bouillon. Having reached the stage of development already described, the bacilli begin to show in the middle of the rod little accumulations of thickened protoplasm, that unite to form a large glistening body which appears as a bright spot of irregular outline in the middle of the cell. This body increases in size and brightness, is surrounded by a well-defined membrane, and is about the same width but somewhat shorter than the bacillus. It is sometimes wider than the cell, and when many of these bright egg-shaped bodies have formed in a chain of bacilli, a striking picture somewhat like a string of pearls is obtained. Presently the transparent remnant of the protoplasm, which has not been used for the formation of the spore, is dissolved and the spore is liberated.

If the spores are now placed in fresh bouillon, they begin to germinate. This process can be watched in a hanging drop of liquid agar, which soon hardens and holds the spore, so that they can be observed during the different stages of their development. The spore soon loses its glistening appearance and increases in length. The tough membrane is next ruptured at one end, and the young bacillus projects from the opening. It continues growing in the direction of the long axis of the spore, and finally casts off the shell of the spore and appears as a completely-developed bacillus. The growth of the bacilli is most active at a temperature of 37° C., the extreme range of temperature being from 16° C. to 45° C. Access of oxygen is necessary. The spores do not germinate at a temperature below 24° C., and they need a large supply of oxygen. Spores do not form, therefore, either in the living body or in the cadaver of an animal which has died of the disease. They grow best artificially on the surface of agar or of potato, or in thin layers of bouillon, or in human urine freely exposed to the air.

The bacilli have comparatively a slight resisting power: they are readily destroyed at a temperature of 60° C., and are unable to live more than a few weeks in the dry state. The spores, however, belong to the most durable of bacterial organisms. It is difficult to destroy them with chemical agents, and when they exist in a state of nature sunlight alone appears to have a destructive action upon them. These spores are used as a standard test of the value of disinfectants, and threads dried in spore-cultures may be preserved for an indefinite length of time and used for this purpose. In gelatin the track of the needle is found filled with a whitish growth, from which delicate white threads project into the surrounding medium. On the surface the gelatin begins to liquefy, and at the bottom of the fluid is seen a slimy white layer of bacteria which gradually settles deeper as the liquefaction proceeds. On the surface of obliquely-hardened agar the bacteria appear as a

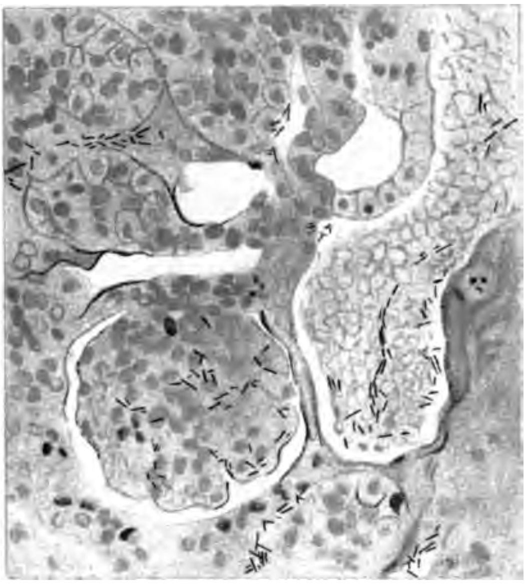

FIG. 21.—Section of Kidney from an Animal dead of Anthrax, showing bacilli in blood-vessels.

grayish-white growth with a dull silver hue and raised somewhat above the surface.

The virus may be introduced into the system in various ways. It may be inoculated even in very small quantities, and will produce a fatal septicæmia, as it is reckoned among the most highly infectious of the bacteria. Buchner succeeded in introducing the spores and also the bacilli into the respiratory passages by inhalation. The bacilli produced much more irritation than the spores, and pneumonia occurred. Baumgarten is doubtful whether this mode of infection occurs outside the laboratory. When taken into the stomach with food the bacilli are usually destroyed by the gastric juice, but the spores reach the intestinal canal. The alkaline character of the secretions and the high temperature give them an opportunity to germinate. They attach themselves to the epithelium and develop rapidly on the surface: the cells are then pushed aside and the bacilli reach the deeper layers of the membrane. Sheep and oxen are particularly sensitive to this form of infection, it being the one which under natural conditions plays the most important rôle. In man the infection most frequently takes place through wounds, and it forms the malignant pustule, but it has also been observed to gain an entrance through the lungs, giving rise to a pneumonia.

One of Pasteur's most brilliant scientific feats was the demonstration of the possibility of protecting an animal from the virus of anthrax by vaccination. It was found that cultures of the bacilli, carried on at high temperatures, were weakened in their poisonous action. The same result could be obtained by growing them at a moderately high temperature for a considerable length of time. Organisms treated in this way were found to produce alkaline substances, whereas the bacilli of natural strength produced acid substances. It was thought that this discovery would prove of great practical value, but experience has shown that, although sheep are protected by the vaccine thus produced from an inoculation with bacilli of full strength, the immunity is not permanent, but lasts only about a year, and, moreover, that it does not protect against infection through the intestinal canal. As this is the most frequent form of infection in cattle, further experiments are necessary to determine whether it is possible to devise a practical system of vaccination of cattle.

An albuminose has been been separated from anthrax cultures in Koch's laboratory by precipitation with absolute alcohol. It was then redissolved and filtered through a Chamberland filter. Injected into animals, it was found to exert a protecting influence.

According to Pasteur, the strength of the anthrax virus may be restored by inoculation into susceptible animals. Cultures from the blood of such animals will have an increased virulence. Cenkowski in Russia succeeded in obtaining an improved vaccine by passing the virus through the marmot (*Zieselmaus*) until a definite strength was obtained. The cultures of this vaccine were preserved in glycerin. Less than 1 per cent. of the animals were killed by the vaccine, and his tables show that during four years of its use, a larger number of animals being vaccinated each year, there was a diminution of the anthrax mortality in the herds from 8.5 and 10.6 per cent. to 0.13 per cent. An examination of the infected tissue shows the bacilli chiefly in the capillary system ; few organisms are seen in the large vessels, whereas the capillaries are crowded. They are found in the spleen, in the liver, and in the kidneys (Fig. 21), particularly the glomeruli. In the capillaries of the intestinal mucous membrane is occasionally found a ruptured vessel through which the organisms have escaped into the surrounding tissue.

It was thought at one time that bacilli were eliminated with the various excretions, but it has been maintained that it was impossible for the bacilli to pass through the walls of the capillaries. Baumgarten is, however, of the opinion that the bacilli are as well able to migrate as are the leucocytes. Inasmuch as the capillaries of the kidneys are filled with these organisms, it is not surprising that the bacilli are found in the urine. It is also quite certain that they can pass through the placenta and affect the fœtus, whether by penetrating through the walls of the blood-vessels or by escaping into the extravasations which are so numerous in the placenta.

Rosenblath inoculated five pregnant guinea-pigs with anthrax. From the nine fœtuses he obtained anthrax cultures in five. As the infection of the fœtus does not always take place, it is probable that the bacilli pass through the placenta only under unusual conditions. The very frequent hemorrhages which accompany the disease probably give the bacilli an opportunity to escape from the circulation of the mother into that of the fœtus.

The bacilli are supposed to exert their pathological action in several ways: First, by so crowding the capillaries as to interfere with the nutrition of the parts; secondly, by robbing the tissues of oxygen; and, finally, by the formation of a toxine which exerts a poisonous influence.

As the spores are the organisms which have preserved this disease from time immemorial, and which make it so difficult, even with our present knowledge, to prevent epidemics, it is interesting to consider how cattle are exposed to their influence. During an epidemic the discharges from the intestine, the bladder, and the nostrils are scattered about on the surface of the earth in the track of grazing cattle. The organisms find a resting-place also in their hides. It was at one time thought that the bodies of buried animals might be a source of infection, but the conditions for germination at some depth beneath the surface of the ground are not found to be favorable. The spores, therefore, find a resting-place only in the superficial soil. They may be freed from their surroundings either by wind or by flood, and, mingled with the food of animals, may become the source of a fresh epidemic. Man is exposed to infection chiefly from contact with diseased animals or from handling their hides or wool; hence the name "wool-sorter's disease" has been given to anthrax in man.

Actinomyces is a form of fungus which was first described by Bollinger in 1877 as existing in cattle, and which Israel found also in man a year later. It did not become generally understood, however, until Ponfick's article appeared in 1882. Bollinger found it in peculiar lumps about the jaws, the throat, or the tongue of animals, which lumps were supposed to be tubercle, cancer, and various other affections. In man the fungus is accompanied more or less by extensive suppuration in the same localities and also in other parts of the body. The organisms seen by the naked eye appear as a growth about the size of a millet-seed: they are yellowish, sulphur-like bodies of a tallowy consistence, which bodies, seen under the microscope, consist of a cluster of straight or of wavy branching threads, and also of radiating prolongations quite thick and clubbed- or pear-shaped, appearing sometimes like the fingers of a hand. These prolongations are so arranged as to give the growth the appearance of a sunflower. The size of these colonies varies greatly, ranging from scarcely visible bodies to nodules 2 mm. in diameter. Their color may also vary from the light yellow mentioned to whitish, light brown, or green, and their surfaces may be smooth or mulberry-shaped. The club-shaped ends may be wanting, and the growth then appears very much like the streptothrix found as concretions in the lachrymal ducts of man. The radiating arrangement of the threads may also be wanting, in which case the growth is not unlike the leptothrix found in the mouth. It has been thought by some that these different appearances indicate a mixed growth of organisms, but culture-experiments prove that this is not the case —that the organism belongs to a polymorphous or cladothrix variety of fungus.

The organism is colored with difficulty. The finer threads take the aniline colors well, but the club-shaped prolongations do not take the staining. They appear to be the result of a retrograde change in the growth. A portion of a nodule is spread upon a cover-glass and is allowed to dry. The glass is then heated in the flame of a lamp, and a few drops of picrocarmine solution are allowed to fall upon it. After two or three minutes the preparation is washed in distilled water and alcohol and examined in water and glycerin. The fungus takes the yellow staining, while the other structures appear red. When sections are examined Gram's method of staining may be used. The actinomyces colonies are then seen stained a bright blue, surrounded by a zone of the clubbed ends colored a pale yellowish-pink; around this a zone of pus and of granulation-tissue colored pink; and, outside of all, the several tissues stained red. Sections may also be stained in Ziehl's carbolic fuchsin for fifteen minutes to half an hour, and then decolorized in a 1 per cent. picric-acid solution until the whole section has a yellow appearance. Dehydrate and

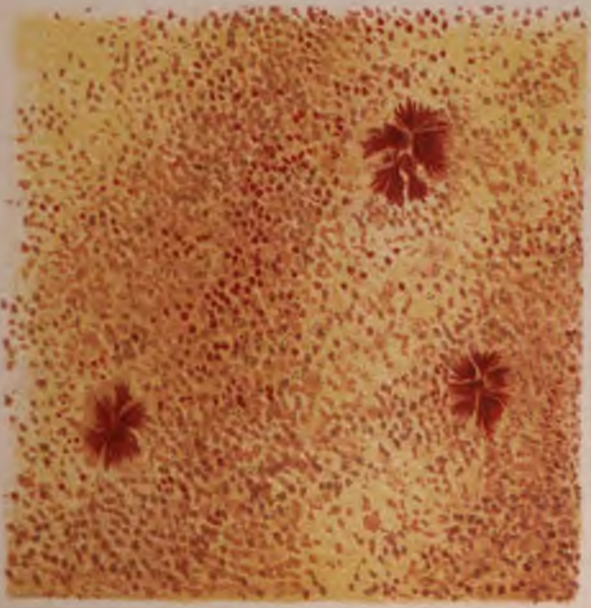

FIG. 22.—Section of Tumor of a Calf, showing actinomyces.

mount. The fungus appears as a brilliant red aster, while the surrounding tissues are colored yellow (Fig. 22).

According to Baumgarten, it is difficult to get a pure culture unless the growth be stirred in liquid gelatin, which is then poured upon a glass to harden. It can thus be grown upon blood-serum, gelatin, or agar. The cultures develop best at temperatures of from 33° to 37° C., and the growth is complete at the end of five or six days. When grown on the surface the line of inoculation widens and has a granular whitish appearance. Presently small, yellowish-red nodules form in the centre of the culture, while the border is surrounded by a delicate white fringe. Finally, the nodules run together and are covered by a white velvety coat.

III. HYPERÆMIA.

Among the most elementary disturbances in the whole domain of surgical pathology, in many cases so slight as hardly to be called "pathological," are those changes in the circulation known as *hyperæmia*. From the earliest times these vascular disturbances have been recognized as the effect of some form of irritation acting upon the organism, as is evident from the phrase "*ubi stimulus ibi affluxus*" handed down by early writers. It was not, however, until Claude Bernard gave the impetus to special research in this direction by his discovery in 1851 of the result of section of the cervical sympathetic nerve that any extended scientific study of the condition was attempted. Since then the science of angioneurology, "one of the most important doctrines in medicine," has been evolved. The importance of a study of this subject need hardly therefore be urged as essential to a proper understanding of some of the more complicated pathological problems which will engage the reader's attention later.

Hyperæmia signifies *an increased amount of blood in a part.* When, on the one hand, there is an increased amount of blood in all the vessels of the body, the condition known as *plethora* exists. On the other hand, anæmia is a term used to denote the condition existing when there is less blood than usual in the body. This term is, however, used in a medical sense to indicate certain pathological changes in the blood. Finally, ischæmia means a decreased flow of blood to a part.

Hyperæmia is of two kinds—*active* and *passive*. In active hyperæmia there is an increased flow of arterial blood to the part. This condition has sometimes been called "fluxion." In passive hyperæmia there is a slowing of the blood-current; the blood is venous in color; a condition of stagnation exists. The condition of the circulation in active hyperæmia is well described in the account of an experiment by Vulpian on the vaso-motor effects produced by faradic stimulation of the peripheral segment of the lingual nerve in a dog. There is a considerable dilatation of all the vessels of the corresponding half of the tongue in the region in which this nerve is distributed. The mucous membrane in this region and also on the corresponding side of the frænum becomes bright red. The principal vein of this part of the tongue becomes turgescent, and the blood contained in it and its tributaries is bright in color, resembling that of arterial blood, while there is a corresponding rise in the temperature of the part.

In active hyperæmia there is an increased rapidity of flow of the blood, not only through the arteries, but through the veins also. If an artificial hyperæmia be produced in a dog's paw by division of the sciatic nerve, there will be found an increased tension in the femoral vein, as shown by a canula inserted into that vessel and placed in connection with a manometer. If the vein be tied, there is an almost arterial pulsation in it. There is, then, in hyperæmia an increased pulsation and dilatation of the arteries and a filling of the veins with arterial blood. Even the smallest arterioles, which do not pulsate ordinarily, begin to pulsate as soon as pressure is made upon them. The condition of the capillary vessels can conveniently be studied in the web or the tongue of a frog. Under normal conditions the capillaries contain but few corpuscles, one or two at a time flowing through, and apparently filling out, the lumen of the vessel; at times only liquor sanguinis is observed. Under a slight stimulus there is marked increase in the rapidity of the flow of the corpuscles, and the little vessels are distended with them, many appearing in the field of the microscope that were not before observed. Both the arteries and the veins are much dilated, and the rapidity of the flow is greatly increased. Whether there is or is not an actual dilatation of the capillaries is still a disputed question, as the absence of muscular and elastic walls in the capillaries does not permit of the marked changes of calibre seen in other kinds of vessels. Stricker, however, has an explanation which enables him to assume that active dilatation and contraction of the capillaries take place. Experiments on the glandular vesicles of the skin of a frog, representing a single acinus and duct, show that under the stimulus of the faradic current the cells which line the acinus swell up and diminish the calibre of the acinus, and that on removal of the stimulus the same cells shrink and enlarge the cavity. A similar swelling of the cells forming the capillary walls has been observed, and the changes in the size of the lumen of these little vessels are supposed by Stricker to occur in this way.

The following, then, are the principal changes seen in active hyperæmia. There is a temporary increase in the amount and rapidity of the flow of blood, and when this has subsided the circulation goes on as before, and no perceptible change in the part appears to take place. Ordinarily, there is no escape of fluid from the walls of the vessels, and if a canula is placed in a lymphatic of the leg of a hyperæmic animal, no increased flow of lymph will be found. Œdema may, however, sometimes occur to a moderate extent, and the wheals of urticaria are supposed to be examples of such a condition. Occasionally there may even be rupture of the vessels and hemorrhage, but this only occurs when there is some pathological complication or when the vessels themselves are diseased. Usually the effect of hyperæmia is quite the opposite; the walls of the vessels, instead of becoming thinner, are actually thicker, having undergone hypertrophy from the hyperæmia, probably of the vasa vasorum.

The increased warmth accompanying hyperæmia is easily explained. The temperature of the surface of the body is always less than that of the interior, as considerable elimination of heat is constantly taking place. Indeed, the variations of temperature on the surface may be considerable. If now an increased amount of warm blood from the interior of the body flows through a given territory, the tissues become warmer and the temperature of the part is raised. Increased nutrition of the part, or increased activity of the muscular walls of the vessels considered as sources of heat, can hardly be sufficient to produce any perceptible local increase of temperature.

The apparatus by means of which these vascular changes are accomplished is known as the *vaso-motor system*. The origin of the vaso-motor nerves or the vaso-motor centres has been traced to the medulla oblongata. The exact spot has variously been stated as at the boundary-line of the cervical and dorsal portions of the cord, or in the anterior portions of the lateral columns, or in the lower part of the floor of the fourth ventricle near the point of the calamus.

These nerves can be divided into two groups. A large majority leave the spinal nerves with the rami communicantes, enter the sympathetic, run upward or downward, and terminate in independent branches of the sympathetic or the splanchnic nerves which supply the abdominal organs; or, after entering the sympathetic, they return through the rami communicantes to the spinal nerves, and are distributed with them to the skin, muscles, and bone. Another group does not enter the sympathetic at all, but takes its course in the spinal nerves. The latter groups are called the "direct supply," and the former the "indirect supply," of vaso-motor nerves. The sympathetic does not form a separate system, but is connected with the spinal nerves. The cervical portion receives fibres from the first dorsal nerve-roots. The nerves which enter the sympathetic for the lower extremities come from the lumbar nerve-roots.

The classical experiments of Claude Bernard gave the first information as to the physiological action of the vaso-motor system. The division of the cervical sympathetic in the rabbit was shown by him to be followed by marked hyperæmia or dilatation of the blood-vessels in the ear. This was finally explained by supposing a paralysis of the vaso-constrictor nerves to have taken place. The same observer, however, discovered that stimulation of the chorda-tympani nerve produced dilatation of the vessels in the submaxillary gland. Here, then, was a demonstration of two different kinds of nerves in the vaso-motor system, one of which by its action constricted the blood-vessels; the other, when in activity, produced a dilatation of the vessels. For a long time the chorda tympani and the nervi erigentes of the corpora cavernosa were supposed to be the only examples of the dilator nerves. Goltz, however, undertook to demonstrate the presence of the vaso-dilator fibres in the sciatic nerve of animals. He found that section of this nerve was followed by dilatation of the blood-vessels of the limb, which after a while resumed their natural calibre. Cutting off a second fragment from the peripheral portion of the nerve reproduced the dilatation. These phenomena were explained by the presence of vaso-dilator nerves which were irritated by the section. Other observers, however, showed that if the peripheral end of the divided sciatic was stimulated there took place a contraction of the vessels, which later gave way to dilatation due to exhaustion; the nerves therefore were constrictors, and not dilators.

Ostroumoff found, however, that in curarized dogs the freshly-divided nerve contracted when irritated, but that three or four days later the same irritation produced dilatation; time, therefore, was an element of importance in the problem. He assumed that both kinds of nerves are present, and that the vaso-constrictors degenerate soon after section, but that the dilators degenerate slowly.

It has been noticed by all observers that the dilatation following section of the sciatic subsides at the end of a few days. This change is said to be brought about by the perivascular ganglia, which, with the nerve-plexus uniting them, are supposed to acquire gradually a higher degree of activity after separation from the nerve-centres.

Such a system of ganglia and nerves has never been demonstrated anatomically; no one has ever seen it, but there is found in the walls of the small intestine a similar plexus of nerve-cells and nerve-fibres, which plexus seems to preside over the movements of that organ, and to be subjected to excitation and inhibition through nerve-fibres connecting them with the cerebro-spinal centres. Microscopical clusters of ganglia have been seen on the arteries of the submaxillary gland, as also in the neighborhood of the large vessels of the penis.

Stricker explains the phenomena supposed to be caused by the local ganglia in another way: he assumes that recovery from hyperæmia following section of the cord is accomplished by nerve-branches which are given off from the cord above the point divided, and which anastomose with the nerves going to that part. These nerve-branches gradually acquire increased power, and eventually exert a sufficiently powerful action upon the dilated vessels to cause them to contract again. This he calls "collateral innervation."

In the light of the investigations which have been quoted we are justified in assuming the existence of the vaso-constrictor nerves and the vaso-dilators, which place the blood-vessels in communication with the vaso-motor centres. A peripheral vaso-motor mechanism also exists, presided over by the so-called "perivascular ganglia." The perivascular ganglia and the vaso-constrictors are continuous in action; they keep the muscular walls of the blood-vessels in a state of tonic contraction, or, in other words, they give them their proper tonus.

The dilators are not always in action, but are called into play only under exceptional circumstances. According to some authorities, these nerves act like the vagus by producing an inhibitory action upon the local ganglia. Others believe them to have the ability to dilate the blood-vessels directly by their own action. Among the latter authorities is Stricker, who has shown that the dilators emerge from the cord through the posterior or sensitive roots. Most physiological and many pathological hyperæmias are, according to him, produced by an irritation of the dilators. The close anatomical relationship between the sensitive and dilator nerves would explain the existence of hyperæmia in connection with many forms of neuralgia and the presence of pain accompanying the congestion of inflammation. He says: "It is probable that the local irritation excites at the same time both the sensory nerves and the vaso-dilators of the implicated region. Whilst the former cause pain by centripetal conduction, the latter produce a dilatation of the vessels by centrifugal conduction."

There may be found however, a vascular hyperæmia produced by purely reflex action. Goltz irritated the central end of a divided sciatic nerve, and obtained sometimes a dilatation and sometimes a contraction of the vessels in the opposite leg. Brown-Séquard and Lombard, after irritation by pricking, found a rise of temperature of a man's skin on the same side of the body, and a fall of temperature on the other side. These changes, though slight, were observed by Lombard's very delicate thermo-electric apparatus, and they indicated contraction or dilatation of the vessels. Numerous examples of this form of hyperæmia may be given. Neuralgic affection of the knee-joint with swelling is observed to be dependent upon uterine disorder. The danger of sympathetic inflammation of the sound eye following injury to either one of the eyes is well recognized. Weir Mitchell has observed a burning in the symmetrical part following injury to a certain portion of the body. A lowering of temperature has also been observed in one hand on placing the other hand in cold water. The application of ice-bags to the heart, the abdomen, and the thighs has produced contraction of the blood-vessels in distant portions of the body. In fact, a system of treatment has been based upon the sensitiveness of the vaso-motors to heat and cold. It is a well-recognized fact that headache may be relieved, that nose-bleed may be stopped, and that the catamenial flow may be established by judicious use of these remedies, and it is not surprising that still greater claims are made for these remedial powers when there is taken into consideration the very considerable disturbances in the distribution of blood to different parts of the body, which disturbances may be produced experimentally. Irritation of the splanchnic nerves, on the one hand, produces contraction of the powerful abdominal blood-vessels and increases greatly the arterial tension throughout the body; on the other hand, division of the splanchnics produces hyperæmia of these vessels. Stricker says: "If this reservoir is wide open, it can contain so large a portion of the total amount of blood that the rest of the body becomes anæmic. An animal with complete paralysis of the abdominal viscera therefore bleeds to death, as it were, into its own abdominal vessels." In this condition there is dilatation of the mesenteric and of the renal arteries. At the same time on division of the portal veins an increased flow of blood is observed. No increase of temperature was found in the abdominal organs after division or irritation of the various nerves and ganglia supplying them, as they already possessed the highest temperature of all parts of the body. Such is the condition of the abdominal vessels in the frog in the well-known Goltz experiment. This experiment consists in tapping the abdomen of a frog with light but frequent blows, which result in a temporary cessation of respiration, heart-pulsation, and muscular action, from which condition, however, the animal speedily recovers. As all local hyperæmias are accompanied by compensatory local anæmias somewhere else to preserve the pressure, it can easily be seen that the blood-vessels of the abdominal viscera can become the regulators of the blood-pressure throughout the body.

As hyperæmia may be caused by paralysis of the constrictors or by irritation of the dilators, *two forms of active hyperæmia* must be recognized. When caused by a paralysis of the constrictors it is known as *hyperæmia of paralysis*, or neuro-paralytic congestion; when caused by an irritation of the dilators it is known as *hyperæmia of irritation*, or neuro-tonic congestion (Recklinghausen). The various elements which combine to form the vaso-motor system tend to counteract one another, and, in disturbances, to restore the normal condition. If a sudden change takes place in one direction, a reaction in the opposite direction may soon occur. After long exposure to cold there is a tendency to congestion of the part; to avoid this, frozen parts must be warmed slowly; conversely, the arm and hand which have been held for a long time in warm water may become paler than usual.

One of the most striking examples of *hyperæmia of paralysis* is observed after gunshot injury of the cervical sympathetic. A case is reported by Mitchell, Morehouse, and Keen that at the end of six weeks showed unilateral hyperæmia of the face after an unusual exertion, with redness of the conjunctiva, contraction of the pupil, secretion of tears, and ptosis. A similar injury recently occurred during the writer's service at the hospital, that was followed immediately by changes in the pupil and hyperidrosis of the injured half of the face and the neck. Hutchinson observed, after fracture of the clavicle, paralysis of the arm, narrowing of the pupil, and rise of temperature of the injured half of the face. Such evidences of pressure on the cervical sympathetic in this injury he considers not unusual. A more extensive form of this kind of paralysis is given by Gröningen. A laborer lying on his back after a full meal was playfully hit upon the stomach with a plank; in fifteen minutes he was dead, and at the autopsy no structural lesion could be found in any part of the body. Many examples of syncope due to blows upon the chest and the abdomen, followed by death or recovery, and usually ascribed to shock, are undoubtedly caused by a reflex paralysis of the heart and the abdominal vessels. As the treatment of these cases is very different from that adapted to shock, it is important that the two conditions should be distinguished from each other. The action of the heart in cases of vaso-motor paralysis can be restored by electric stimulation or frictions and by compression of the abdominal walls to force the blood forward into the heart, whereas in shock absolute rest is of the utmost importance.

But few examples of hyperæmia of paralysis are recorded as following injuries of the nerves of the extremities. An observation by Waller on the ulnar nerve is worth mentioning here: The nerve at the bend of the elbow was placed on a freezing mixture until all sensation was lost. A rise of temperature with congestion was then noticed in the skin between the third and fourth fingers, and in some cases this condition lasted several days. Swelling of the finger-joints has been noticed following fracture of the internal condyle of the humerus causing pressure on the ulnar nerve. The same condition sometimes follows Colles's fracture, and is probably produced by pressure upon the nerves of the wrist by the displaced upper fragment.

The *hyperæmias of dilatation* are, as a rule, shorter and quicker in their action. They are accompanied by nervous symptoms, such as neuralgic pain, active secretion of the gland supplied by the nerve, œdema, and desquamation of epithelium from membranes. The changes of color in the cheek following disturbance of the emotions, as shame or anger, are regarded as examples of this form. The flushing following the stimulating effects of alcohol, tea, and coffee is supposed to be due also to stimulation of the dilator nerves. Redness of the conjunctiva, and even of the forehead and cheek, with flow of tears, is an occasional accompaniment of facial neuralgias, and is a symptom in accord with observations of Stricker on the presence of the dilators in the sensory roots. In fact, in hemicrania a dilatation of the vessels of the retina, both arteries and veins, has been observed. Perhaps the most striking example of hyperæmia following nerve-irritation is herpes zoster. Not only does the eruption follow the anatomical distribution of nerves, but evidences of inflammation have also been observed in the nerves themselves by Haight and others.

Cases of erythema, described by Mitchell, Morehouse, and

Keen, following irritation of nerves previously severed by gunshot injury, are probably due to an active dilatation of the vessels. Redness and swelling of the joints have been observed by Weir Mitchell in cases following gunshot injury of the brachial plexus, and by Packard in a case of compression of the sciatic nerve by a tumor. The conditions described by Mitchell as erythromelalgia may be classed with these hyperæmias. The reflex hyperæmias are said by Reckligh ausen to belong to this class also.

Hyperæmia caused by *paralysis of the perivascular ganglia* may be observed in parts of the body separated from the nervous centres, as in transplanted flaps, where an unusual susceptibility to heat and cold is ordinarily shown by changes in the calibre of the vessels. A hand and forearm separated from the nervous centres by division of the nerves exhibited this increased susceptibility: on dipping the hand into cold water congestion with the formation of vesicles took place. A bright blush suffuses a limb after removal of an Esmarch bandage and the capillary hemorrhage from the wound is for a short time quite active if means have not been taken to prevent its occurrence. The dilatation of the blood-vessels is here evidently due to a local influence exerted directly upon them, either as the result of pressure or the removal for a certain length of time of the nutrient blood. Whether this local influence is exerted partly upon the muscular apparatus of the vessel-walls directly, and not through the perivascular ganglia, is an open question. The congestions of the walls of sacs following evacuation of their contents belong to this class. Tapping the abdomen for ascites may be followed by heart failure or by serious hemorrhage into the peritoneal cavity if the pressure of the fluid is not replaced by external support. Too rapid evacuation of a bladder distended by obstruction from enlargement of the prostate may be followed by hæmaturia and cystitis. In such a case the vessels of the bladder-wall are suddenly deprived of a support to which they have been accustomed for months or for years perhaps, and have lost the tonus which enabled them to preserve their normal calibre. This rapidly-produced hyperæmia is followed by rupture of some of the vessels or by a congestion terminating in inflammation. A portion only of the urine should be removed from such a bladder in order to allow the blood-vessels time to regain their tonus. A similar condition is often seen in limbs after fracture. The distention of the blood-vessels so characteristic during the first attempts to place the foot upon the ground after prolonged rest in the horizontal posture is in part due to increase of pressure from the vertical position. The relaxing effect of moderate heat upon the vessels of the hand on placing it in warm water is familiar to every one. Very hot water will stimulate the constrictors, and is therefore useful in arresting hemorrhage from a wound. Prolonged douches of hot water have a similar astringent effect, and are used upon the cervix uteri for this purpose. The class of remedies known as *rubefacients* have probably a local action only on the blood-vessels; when very stimulating they will produce primary constriction followed by dilatation of the vessels. It is supposed that many of the erythematous eruptions seen in bacterial diseases, such as, for instance, surgical scarlet fever, are produced by the local action of the bacteria or their toxic products upon the vessels. The artificial congestion produced by cupping is not a pure example of either active or passive hyperæmia, as the vacuum draws the blood from all quarters indiscriminately; that is, partly from the arteries and partly from the veins.

Hyperæmia is, as a rule, a passing condition, and, as already stated, leaves the part in the condition it was before; long-continued hyperæmia may lead to hypertrophy of the vessels, and also of the part itself, as hypertrophy of the heart from hyperæmia of the coronary arteries. When dilatation of the blood-vessels comes on suddenly and is intense in character, there may be an exudation of plasma from the vessels and œdema will take place. This is particularly noticeable in soft tissues, as the eyelids, in the neighborhood of inflammations, and is known as *collateral œdema*. It is probable, however, that in these cases there is not a pure example of hyperæmia, but that other elements are at work, of which more will be said when studying inflammation. Œdema, and even hemorrhage, may, however, occur as the result of pure hyperæmia, as is seen in many forms of skin eruption. At times excessive glandular secretion occurs: this is observed in the mucous membranes and also in the skin. It is a question whether the secretion is the result of a reflex irritation of the nerves going to the gland-cells or of the dilatation of the blood-vessels of the gland. In very chronic cases there is found, in addition to hypertrophy, an unusual growth of hair on the part.

Passive hyperæmia is caused by partial or by complete obstruction of the flow of blood through the veins. It can be produced artificially by placing a ligature around a large vein. If this vessel be placed in communication with a registering apparatus, it will be found that there will be considerable increase of pressure at first, but that in a short time the pressure has returned to normal.

The blood has found its way around the obstruction through the neighboring veins, which exist in abundance. If, however, a tourniquet is placed around a limb tightly enough to obstruct only the veins, but not the artery, there will soon be seen a rise in the pressure, which will become almost equal to that in the arteries. There may even be a pulsation in the veins. The same condition will be established after obstruction of a single vein in organs which have only one vein, as the kidney. Obstruction of the portal vein and of the femoral vein under Poupart's ligament will also be attended by such serious disturbance.

In this form of hyperæmia the color of the skin will be bluish or dark red. When the surface is unusually transparent, as under the nails, there is a livid or cyanotic hue. The change of color is most marked at the extremities, where the capillaries are large, or where the arterioles terminate in veins without an intermediate capillary system. The temperature of the surface is cooler than usual, this being due to the slowing of the blood-current, thus allowing less warm blood than usual to pass through the tissues. The venous color appears to be due in part also to this state of the current, for the blood remains longer in the part, and consequently becomes more highly charged with carbonic acid and more completely deprived of its oxygen. In amputation wounds the venous color of the blood flowing from the surface is marked while compression is still partly exerted by the tourniquet, and the flow is more rapid than normal, owing to the increased pressure in the veins. Such hemorrhage will, however, speedily be arrested by removing the tourniquet and allowing the current to flow in its natural direction toward the heart.

The minuter changes in passive hyperæmia may be studied in the frog's tongue after tying the veins on either side. There is at first an appreciable slowing of the current in the small veins and in the capillaries. These vessels soon become filled and distended with blood-corpuscles, the plasma-layer in the smaller veins disappearing entirely. The red corpuscles now appear to lose their contour and become fused together in an almost homogeneous mass. The flow of blood ceases, and the blood-column has a rhythmical pulsation communicated to it with each heart-beat. Presently at isolated points red corpuscles appear projecting through the walls of the capillaries and small veins, and finally they are forced completely through, owing to the pressure to which they have been subjected. There is at the same time also an escape from the vessels of a certain amount of fluid, which gives rise to œdema caused by the pressure exerted upon the small vessels both by the veins and the arteries. In the arteries no increased pressure is observed, as their tonus is always higher than any pressure that can be produced by this form of hyperæmia.

A study of the arteries of the retina shows that they are narrower than usual under these circumstances. This contraction of the arterioles is supposed to be either compensatory, so as to bring less blood to the congested part, or is for the purpose of making the blood-stream more powerful. The exuded fluid is poorer in albumin than the liquor sanguinis or pure lymph; and it has but slight tendency to coagulate. The reddish tinge sometimes given to the fluid is due to the presence of red corpuscles.

One of the most familiar examples of this form of hyperæmia is that condition of the vessels of the lower extremities accompanying varicose veins. Here all stages of the process can be studied. At first there is only œdema, the change in color being but slight, owing to the collateral circulation. Later there is considerable pigmentation of the skin, owing to the destruction of the escaped red blood-corpuscles, and finally the disturbance in the nutrition of the part is so great that a breaking down of the tissues takes place and gives rise to ulceration. Many of these symptoms can be made to disappear by overcoming the obstruction due to the dilated and tortuous blood-channels, which can easily be done by placing the limb in a horizontal posture. Passive hyperæmia may also be produced by pressure on venous trunks from inflammatory new formations or tumors.

If the force of the blood-current is naturally weakened, as in feeble individuals or in disease of the heart, there may be local congestion at points where it is most difficult for the blood-column to overcome the force of gravity. This congestion often occurs in the lungs when an enfeebled individual has been for a long time in the recumbent posture, for then the blood-pressure is always more feeble. These forms of hyperæmia are known under the name of *hypostatic congestion*. It is possible that such congestions may take place in other internal organs, such as the prostate and bladder. It is necessary to be on guard against complications of this kind when confining the aged to bed for any length of time. A similar condition is that which leads under similar circumstances to decubitus or bed-sore. Light pressure on a spot for a considerable time causes an ischæmia which is followed by a relaxation of the vessels, particularly the small veins, owing to the feeble circulation, instead of the usual hyperæmia that in the normal condition should follow. The most protruding portions of the skeleton posteriorly indicate the points where these congestions are likely to occur. The feeble circulation is followed by stasis in the capillaries, the stage preceding actual death of the part, which stage may occur in the form of ulceration or gangrene. The bluish color imparted to portions of the body subjected to great cold is due to hyperæmia following an ischæmia of the part. In parts which have been in a state of chronic inflammation slight external influences will produce the cyanotic color for the same reason. The hyperæmia and swelling in legs convalescing from fracture is in part due to passive hyperæmia. In heart disease there may be general passive congestion of the whole body, as well as anæmia, and in shock the pallor, the clammy and cyanotic skin, are all due to a feeble heart-action which slackens the blood-current in the capillaries and the veins.

IV. SIMPLE INFLAMMATION.

1. The Process.

A proper understanding of the phenomena of inflammation may be said to be absolutely essential as a basis upon which to build up a knowledge of surgical pathology. The close relation of the blood-vessels to the inflammatory process was recognized by Hunter, who says: "The act of inflammation would appear to be an increased action of the vessels." He recognized the congestion of hyperæmia accompanying inflammation "as the first act of the vessels when the stimulus which excites inflammation is applied."

In a study of the circulation as observed in inflammation, the experiments of Cohnheim, both on the circulation and the action of the white corpuscles, first published in 1867, added greatly to the knowledge of this process, and deserve, therefore, to be mentioned first. Such modification of his views as were suggested by other observers will be then considered. If a frog be paralyzed with curare, and there is drawn through an incision made on one side of its abdomen a loop of intestine, and so spread out that the light can easily be transmitted, there will be obtained a transparent, highly vascular membrane which soon becomes inflamed upon exposure to the air. It does not require very careful observation to perceive that the rapidity of the flow of blood is greatly increased, and that the number of the vessels is also apparently increased, many now being visible which were not before observed. The capillaries, through which there flowed only occasionally a corpuscle, are now quite full and their situation easily determined. The increased rapidity of the flow lasts only for a short time, however, and it is followed by a slowing of the current, which now becomes slower than normal. Thus far, the phenomena observed have not differed in any way from those seen in active hyperæmia; but now a new element, the slowing of the current, is introduced, and from this time on the picture changes, and new phenomena are seen which have not been found to exist in hyperæmia. In consequence of the slowing of the current the corpuscles accumulate in great numbers in the capillaries, which, although distended, do not become materially increased in calibre.

Along the walls of the small veins there may now be noticed an accumulation of white corpuscles. They are no longer swept back again into the current after a temporary adhesion to the wall, but remain attached to the wall until a considerable number have accumulated. Occasionally one is dislodged, only to be soon arrested again in its progress. Finally, their number becomes so enormously increased that the entire vessel-wall appears to be lined with a layer of white corpuscles (Fig. 23). Adherence of white corpuscles to the wall is observed also in the capillaries, but there they are more freely mingled with the red corpuscles, whereas in the veins the two varieties of cells seem to have separated from one another. In the arterioles there is a tendency to accumulation on the inner wall of white corpuscles, this being particularly noticeable during the diastole; the succeeding wave, however, sweeps them back into the current again, and they disappear.

FIG. 23.—Blood-vessel, Mesentery of a Frog, showing diapedesis of leucocytes.

Presently slight protuberances are noticed here and there on the outer walls of some of the small veins, and they gradually increase in size. At corresponding points on the inner side of the vessel are situated white corpuscles. At points favorable for observation one can see that an enlargement of the outer protuberance keeps pace with a diminution of the size of the corpuscle previously observed attaching itself to the inner wall, and that when the corpuscle has entirely disappeared there is seen on the outer wall a perfectly-developed cell, which proceeds to detach itself from the vessel and by frequent changes of shape to change its position from time to time. When at rest these cells are round, granular bodies, containing one or more nuclei, and are not to be distinguished from white blood-corpuscles; when in motion they possess one or more prolongations and become quite irregular in shape, resembling in all respects the "wandering cells" of the connective tissue originally described by Recklinghausen. In the mean time large numbers of similar cells are making their way through the walls of all the veins within the field of vision until they are surrounded with several layers of white corpuscles.

The white corpuscles are also seen escaping through the walls of the capillaries, but to a less extent; and there is found here mingled with them a certain number of red corpuscles. In the arterioles no such passage of cells is taking place, the interior of the vessel-wall, as has been stated, being kept clear of white cells by the force of the current. At the same time there is considerable exudation of fluid from the vessels into the meshes of the surrounding tissue. The mesentery is now distended by a mass of cells and fluid, which presently escapes from the tissues to the surface, where the fluid coagulates and forms a membrane, between the fibrils of which are imprisoned the white and perhaps also some red corpuscles. The escape of white corpuscles from the vessel was first described in 1841 by Dr. Williams in England, but it was not until Cohnheim had so clearly demonstrated the process and its bearing upon the theory of inflammation that it was accepted by the scientific world.

The tongue of the frog, in which has already been observed the changes of hyperæmia, is also well adapted for studying the conditions of the circulation in inflammation. A caustic substance of some kind applied to the centre of the organ will enable one to observe different degrees of inflammation at different distances from the point of injury. On the extreme periphery the circulation is normal; next, a zone of dilated vessels with slowing of the current, and, still nearer, an exudation of white corpuscles is seen, particularly from the veins. As the centre is approached the circulation becomes slower and the exudation greater, until the zone of stasis is reached where the vessels are acted upon by the chemical substance and the blood has coagulated in them.

The different phases of the circulatory disturbances may be produced by simply placing a ligature around the frog's tongue and removing it at different periods of time. If left on from twelve to twenty-four hours, and then removed, a passing hyperæmia is produced. This can be seen on any limb after the removal of an Esmarch bandage. If the ligature is left in place from thirty-six to forty-eight hours, there is caused at first a hyperæmia, followed by a slowing of the current and an exudation of cells and plasma. If left on for sixty hours, the stream will become so sluggish that there will be an enormous diapedesis of white corpuscles, and many red corpuscles will also be found in the exudation. The tongue looks as if it were covered with red spots. If the ligature be not removed for two or three days, the blood penetrates into the beginning of the arteries, but not into the smaller arteries or capillaries or veins, and the circulation is never re-established.

It is quite evident that there is here something different from simple hyperæmia; not only is the current slower, but there is an exudation or a leakage through the walls of the vessels. This exudation is attributed by Cohnheim to a molecular change in the vessel-wall, a condition bringing about different relations of friction and adhesion between the blood and the walls due to changes in the endothelium. Cohnheim thinks that he can exclude the nerves, for he has been able to produce inflammation in the ear of a rabbit when every connection has been severed except the artery and the vein. This, however, can hardly be received as satisfactory evidence, for the perivascular ganglia are not excluded, and it is probable that in a case such as this they may be called into action. The dilatation is also greater than in hyperæmia; for instance, a rabbit's ear will have a still greater dilatation and injection of the vessels after section of the sympathetic if the part be irritated with croton oil or dipped in hot water. The slowness with which the process develops is against the hypothesis of nerve-action; sometimes hours elapse after application of a caustic before any change occurs.

Cohnheim argues, also, that the disturbance is not in the blood, for it may be produced in the tissues while the blood is absent. If the blood be excluded from a rabbit's ear by an Esmarch bandage, and the ear be dipped in moderately hot water, and the ligature be removed as soon as the ear has cooled off, the symptoms of inflammation will presently show themselves, and the ear will become swollen to several times its normal thickness. The disturbance has not been produced in the blood, but in the part itself. It is not probable, he thinks, that the cells of the part can have any influence upon the corpuscular elements of the blood, although it can be conceived that they may attract to themselves the fluid portion. He is therefore driven to the conclusion that *the change is in the wall of the vessel.* It has already been noted that if the blood is excluded from the vessels for a certain length of time, it will not enter them again, although the vessels are apparently open. It would not, therefore, be difficult to understand how under other circumstances these walls can hinder or retard the flow of blood. The chemical character of the fluid which filters through the wall, as compared with that observed in hyperæmia, is another reason for assuming a change in the wall.

This idea of change in the vessel-wall is accepted by Burdon

Sanderson. The vessels dilate, he says, because they have lost the power they before possessed of resisting dilatation. There is a loss of vital power, in consequence of which leakage also takes place. Professor Glax of Graz showed that by keeping up the vital properties of tissues in animals by the artificial circulation of properly arterialized blood through the vessels under an absolutely constant pressure, the introduction of a small percentage of injurious substances, such as metallic salts, produced a leakage and a diminution in the quantity of blood flowing through a given part.

Landerer contends that the *primum movens* in inflammation, or the first thing to be noticed, is the much more frequent injury to the tissue-cells than to the vessels. He would not do away entirely with the view that the vessel-wall takes part in the process. The capillaries should be regarded as vascular spaces in the tissues lined with endothelium like the lymph-spaces, and not as separate tubes sufficiently strong to support all the pressure that may be brought to bear upon them from within. The greater part of the tension is borne by the tissues, which, in virtue of their elasticity, can be placed in a state of elastic tension in the same way as the walls of larger arteries. The irritant[1]—or, as Landerer prefers to call it, the "inflammation-excitor"—exerts an influence upon the tissues in virtue of which they become relaxed; they are thus more easily distended and their elasticity is less complete. This diminished elasticity of the tissues would act upon the momentum transmitted to the blood in the same way as the wall of an atheromatous artery. The pressure cannot be returned to the blood-column, but must be expended in stretching the tissues. The momentum of the blood-column is thus partly lost and diverted to other purposes. The amount of blood increases, but the power to move it diminishes; there is a leakage of lymph, owing to the diminution of external pressure. Landerer thinks that the old phrase, *ubi stimulus ibi affluxus*, which has something mysterious about it, should be discarded, and it should be replaced with the simple physical law of "local diminished pressure or resistance, increased flow."

One of the earliest theories about the circulation was called the "attraction theory," which assumed an increased adhesiveness in the elements of the blood to one another and to the vessel-wall. Another theory assumed a change in the plasma by which it became more concentrated, and thus caused resistance to the natural blood-flow. Or it was thought that there was a vital attraction

[1] Landerer rejects the term "irritation" as too suggestive of nerve- or muscle-action.

of the tissues for the blood : an increase of this function would hold back the blood in the tissues and produce a determination of blood to an organ. An affinity between the fluids of the tissues and the contents of the vessels undoubtedly exists. A change, therefore, in the tissues would affect the blood and the vessel-walls. The action of the cells in inflammation and their power to attract materials from the blood was especially dwelt upon by Virchow.

Recklinghausen does not accept the experimental evidence showing a slowing of the current in inflammation. At the height of the process the color of an inflamed part is scarlet. The color of the blood when drawn by leeches is arterial, and the flow after an incision is more rapid. The pulsation of large arteries is stronger near an inflamed part, and the blood flows away as rapidly as it comes, as is shown in cases of venesection, where the blood from the vein has frequently also an arterial color. The stasis seen in the web of a frog's foot as the result of an "irritation" is not, he maintains, a symptom of inflammation. The irritant always produces at first an increased rapidity of the stream. When very small injuries are produced, there is no slowing of the stream; after a few hours the normal circulation is restored. If strong irritants are used, there is always a zone of "active congestion" or increased rapidity of flow of the blood surrounding the spot. The stasis in the centre leads to necrosis, a result which does not necessarily form a part of inflammation. The purulent softening which occurs around the necrosed portion takes place in the zone of active congestion. In the mesentery of the frog, as Recklinghausen shows, there are many complications which produce a slowing of the current. Among these complications may be mentioned the thinness of the membrane exposed to the air, the contraction of the intestine, the great hyperæmia of the abdominal viscera, and the diminished heart-action and blood-pressure caused by curare. In the frog's tongue which is turned over and stretched out there are frequent obstacles to the blood-flow.

Recklinghausen evidently does not regard the slowing of the blood-current as a necessary part of inflammation. He is, however, willing to admit that some inflammation-excitors may act through the blood upon the vessels, and thus impair the action of their walls.

At all events, it may be concluded, from the experiments described above, that there is produced a condition differing from simple hyperæmia. The disturbance of circulation in inflammation comes on later and lasts longer than in hyperæmia. There is also exudation which does not occur in hyperæmia or occurs only to a slight degree.

In its earliest stages the congestion of inflammation differs probably but little from active hyperæmia. As the process develops there is a greater dilatation of the vessels and a diminution of tension; the vessel-walls and the tissues are "relaxed" through the action of the inflammatory agent. As a consequence, the conditions of hyperæmia are so far departed from as to produce a leakage of the vessels. Should the inflammatory agent occasion a more profound impression upon the part, there may be a temporary stasis in some of the capillary vessels; and there can easily be imagined permanent stasis in a very limited area without the occurrence of necrosis or even of serious disturbance of nutrition.

In the average case of pronounced inflammation there probably exists the phenomena of genuine hyperæmia of the blood-vessels in the peripheral portions of the inflamed mass, with greater distention and relaxation of the vessel as the centre is approached. These causes, combined with the swelling of the parts, would undoubtedly impair the rapidity of the blood-flow. The phenomena of a rapid current, as arterial pulsation and color, with more rapid flow of blood from an incision, might coexist with a slowing of the current in another portion of the same part.

It is a well-known fact that in certain inflammations the congestion may be so severe as to obstruct the circulation of a considerable area, and to an extent that will cause death of the part or mortification. Such severe forms of inflammation are, however, fortunately, extremely rare, and they occur usually in parts not capable of rapid distention, as the bone, or where the circulation is less active, as the extremities of the arterial circuit. The disturbances of circulation of the blood seen in laboratory inflammations must, therefore, be regarded as partly artificial in character. In reality, however, there is probably considerable variation in the rapidity of the blood-flow.

A word may be said here about the changes seen in the *blood* during inflammation. Much attention has been drawn of late to the so-called "third corpuscle," which is a colorless protoplasmic disk from 1.5 to 3.5μ in diameter, these corpuscles numbering, according to Osler, about one to every twenty red corpuscles. They are visible in the circulating blood, and on the withdrawal of blood from the circulation they tend to adhere to one another, and to form irregular granular clumps, known as

"Schultze's granular masses," or as granular débris so often seen in the neighborhood of blood-clots. The name now usually given them is "blood-plaques." Their tendency to agglutinate and to disintegrate has prevented their earlier recognition. They are more numerous in the infant and in the aged. They are supposed by some to be true hæmatoblasts—that is, bodies from which the red corpuscles are formed; they are seen in large numbers when blood-corpuscles are forming, but their relation to this process is still doubtful.

The blood-plaques are much more numerous, however, in acute sthenic fevers and in chronic wasting disease, and probably also in

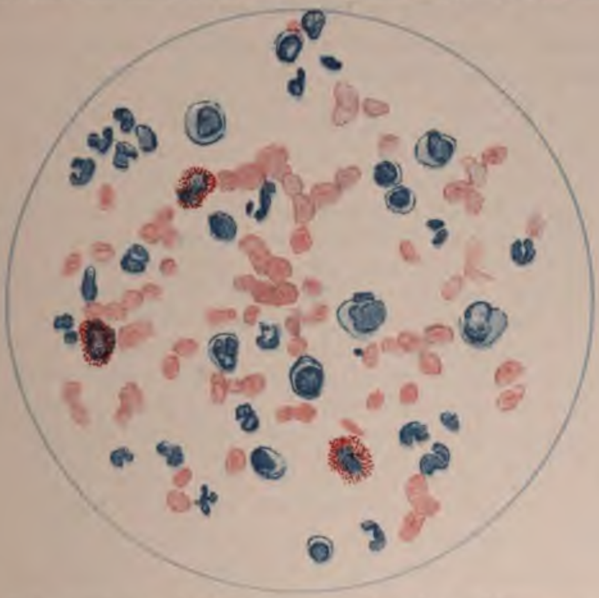

FIG. 24.—Leucæmic Blood, showing various forms of leucocytes.

cases of inflammation, both acute and chronic. At the crises of fevers and after the healing of acute abscesses they are seen in large numbers, and it is supposed by some that an effort at the repair of the blood is thus made by these bodies at this period, but, as has been said, the evidence on this point is yet insufficient. There is a very noticeable increase in the number of *white corpuscles in the blood* during inflammation. This increase is what should naturally be expected from observation of the great increase in the number of these cells in the inflamed part, and from the active migration which takes place through the walls of the blood-vessels (Fig 24). The whole system thus appears to sympathize with the local condition, and those organs in which leucocytes abound, as the spleen and the lymphatic glands, are found much enlarged at this time. Davidson of Edinburgh explains the increase of leucocytes in the blood by a muscular contraction of the spleen, such as occurs in digestion through reflex action from the stomach; in inflammation the source of the reflex irritation is supposed by him to originate in the walls of the arterioles of the inflamed part. These cells appear to be quite independent of the red corpuscles, which were formerly supposed to be derived from them. It will presently be seen that they have quite different functions, intimately connected with the process of repair and the protection of the body from invading organisms.

Leucocytosis is usually seen in the suppurating forms of inflammations, and is of value as confirmatory evidence in the diagnosis of deep-seated abscesses, even the pus of a felon being sufficient to cause marked increase in white cells. According to the observation of R. C. Cabot, it is regularly, though not invariably, present in purulent but not in catarrhal appendicitis, and is of value in enabling the physician to distinguish this affection from colic or from constipation. Leucocytosis may help one to distinguish pyosalpinx and pelvic abscess from pelvic neuralgias and small ovarian tumors. Cabot did not find leucocytosis following urethral fever or cystitis or endometritis. He found this condition of the blood in three cases of suppurative colangitis, but absent in two cases of gall-stones without pus. Leucocytosis was not observed in tubercular affections. In general septic peritonitis it is occasionally absent. It is seen in suppurative osteomyelitis, and also in all forms of suppuration with pocketing of pus following operations. It is the rule in erysipelas. In new growths it is very variable, apparently accompanying chiefly those cases in which cachexia is most marked.

In old times, when venesection was a common procedure in inflammatory disease, it was well known that blood coagulated quickly when withdrawn from the body. The so-called "buffy coat," the *crusta phlogistica*, or white layer, which was seen at the top of the coagulum in a vessel, was supposed to be due to an excess of fibrin in the blood; a fibrinous crasis was supposed to be evidence of an inflammatory state of the blood. It is now known that the white corpuscles play an important part in the process of coagulation. *Fibrin* is formed by the union of two substances, fibrinogen and paraglobulin, with the co-operation of fibrin-ferment. Fibrinogen is found in the blood-plasma, while the other two substances are, for the most part, found in the white corpuscles. When the latter break down these substances are set free, and are able to act upon the fibrinogen and form fibrin. The increased amount of fibrin seen in the coagulum and in the exudations must be ascribed, therefore, to the increased number of white corpuscles circulating in the blood and finding their way into the tissues of inflamed parts.

There is now to be considered the action of the *tissues* of the inflamed part. Before Cohnheim's and Recklinghausen's investigations the increased number of cells found in inflamed tissues was supposed to be due to a proliferation or a multiplication of the cells of the part. This was the view of Virchow, who showed that the tissue-cells are placed in a condition of increased activity by the inflammatory irritant, and consequently attract to themselves nutriment in unusual quantity for their growth and multiplication. The vascular changes in inflammation he regarded as the result of this increased activity of the cells.

In connective tissue there exist two principal varieties of cells —the *fixed* and the *wandering* cells: the former are stellate or fusiform, and lie hidden among the fibres which constitute the principal portion of the intercellular substance. In addition to these there are the small round cells, containing one or more nuclei and a granular protoplasm, in all respects resembling the white corpuscles of the blood. It was Recklinghausen who first recognized their power to take on changes of shape, such as are characteristic of the amœba, and by this amœboid movement (Fig. 25) to change their location. These cells, described by him as *wandering cells*, are constantly moving through the meshes or lymph-spaces of the tissues, entering them from the vascular system and escaping through the lymphatics, keeping up in this way a constant circulation. In the normal tissues they are few in number, and are seen and studied only after careful methods of preparation, but when the tissues are irritated or inflamed they are found there in large numbers, and their presence is accounted for in the way which has already been described when studying the action of the vessels in inflammation. In consequence of these observations Cohnheim assumed that the old theory of cell-proliferation would have to be abandoned in favor of the migration theory. He endeavored to show that the fixed cells of the part underwent

FIG. 25.—Amœboid Movements of a Leucocyte.

no active change during the inflammatory process, and for this purpose made a series of investigations upon the cornea, a form of tissue simple in composition and convenient for study, owing to its great transparency. The cornea when examined fresh in a drop of aqueous humor is seen to be absolutely transparent, and no structure can be distinguished, but when treated with a solution of chloride of gold a beautiful network of large stellate anastomosing cells is seen lying in a transparent intercellular substance. If, however, the cornea be treated with a solution of nitrate of silver, the cells appear as a branched system of canals anastomosing in a dark background. Such pictures as these suggest the presence of spaces through which it would be possible for wandering cells to migrate. It will be well to devote a moment to the consideration of these experiments, as the results obtained by Cohnheim have been the object of much discussion and dispute. They were, in brief, as follows: A ligature is drawn through the bulb of a rabbit's eye, and opacity of the cornea is seen in twenty-four hours, in frogs in from two to six days. Later, the cornea becomes milk-white or grayish or yellowish-white, and thicker and somewhat softer than in the normal condition. This opacity is due to leucocytes. On removing the cornea before the opacity is too great, and putting it into a neutral solution on an object-glass and examining it with a high power, the leucocytes are seen in all shapes, and also the corneal cells with their characteristic prolongations. The leucocytes may be seen moving about independently of these cells, and generally obscuring them. If, however, the cornea is treated with chloride of gold, the corneal cells are seen unchanged. Such changes as have been observed in them by others Cohnheim regards as degenerative only in nature. There is a granular condition of the protoplasm, a retraction of the prolongations, and the formation of vacuoles. If the centre of the cornea of a winter frog is touched with a pencil of nitrate of silver, at the end of twenty-four hours an opaque streak is seen projecting from the margin of the cornea in one or two places, generally from the upper and lower margins, at which point more or less hyperæmia of the vessels is seen to exist. These opacities reach the cauterized point on the third day, and by the sixth day the opacity has localized itself around the cauterized point, while the surrounding cornea is clear. Under the microscope the corneal corpuscles were found by Cohnheim in all cases to remain unchanged, the opacity being due to the presence of large numbers of leucocytes.

One of the peculiarities of the leucocyte, about which more will be said later, is its power to appropriate foreign substances, which thus become imprisoned in its protoplasm. Cohnheim undertook to prove that the new cells seen in the cornea were identical with the leucocytes, by injecting granules of carmine or aniline blue, held in suspension, into the lymph-sacs and blood-vessels of the frog, and subsequently producing a keratitis. In such an inflamed cornea many of the new cells are found to contain these granules, which are not seen in uninflamed tissues. These views, first propounded by Cohnheim in 1867, produced a profound sensation, altering as they did very materially the then existing ideas of cellular pathology. It is needless to say that they met with active opposition from many quarters, but by no one were they so vigorously opposed as by Stricker of Vienna. This observer not only maintained the old theory of "proliferation," but developed it still further and evolved his theory of "tissue-metamorphosis," which, in brief, is that not only the cells, but also the entire tissue, returns to an embryonic condition and separates into amœboid masses; in other words, that the intercellular substance as well as the cells may take part in the formation of new cells in inflammation.

Many other observers also undertook to show that the fixed cells were capable of proliferation, and the cornea was selected for this purpose. Burdon Sanderson, while admitting that immigration plays an important part in keratitis, pointed out that changes in the stellate cells of the cornea could be observed if studied at an earlier stage than that employed by Cohnheim. Shakespeare of Philadelphia recognizes four different kinds of cells in the cornea. His studies show pretty conclusively that the fixed cells are active in the processes of destruction and repair. He goes so far as to say that slight injuries of the cornea may be repaired entirely by these cells without the assistance of the adjacent blood-vessels other than an additional supply of blood-plasma.

Finally, the following experiment would seem to leave little doubt that the corneal cells can proliferate. A cornea is irritated and then excised and preserved in a moist chamber; in two or three days a formation of wandering cells takes place at the point of irritation; the appearances of ordinary keratitis follow. It is certainly fair to infer that these cells came from the elements of the cornea existing there at the time of irritation. Recklinghausen states that changes in the corneal corpuscles have occurred under the eye of the observer, and that fragments of protoplasm separated from them have been seen to go through the same changes of form as wandering cells.

In the omentum of young animals there is a very simple form of epithelium and one more or less remote from blood-vessels. If an artificial peritonitis be produced, Cornil and Ranvier have shown that an active proliferation of these cells will be seen at the end of twenty-four hours. In the writer's own studies of inflamed tissue he has seen undoubted evidence of proliferation of the fixed cells. Some beautiful examples of this were observed in the skin adjacent to a carbuncular inflammation. In the inflammation of the walls of the artery of a horse, produced by the application of a ligature, the muscular cells of the media were seen in an active state of proliferation. Cohnheim in answer to observations of this kind pointed out that many of these changes seen in fixed cells were of a degenerative character and preceded the final destruction of the cell.

The emigration theory still continued dominant, however, until Strassburger, Flemming, and others demonstrated the changes seen in the nucleus known as *karyokinesis*, or indirect cell-division, which they observed in vegetable cells, in the tissues of the lower animals, and afterward in the normal human tissues, and finally also under pathological conditions. (See page 218.) This proved conclusively that the fixed cells did not play a passive part in inflammatory processes, and the rôle which these cells played in hypertrophy, repair, and tumor-growth (Fig 26) was shown to be a more prominent one than had hitherto been supposed.

In any acute inflammation the tissue-cells break down in large numbers; but many of them, according to Ziegler, become wandering cells, and are difficult, at first, to distinguish from leucocytes. They do not produce any pus-corpuscles, but eventually play a prominent part in the process of repair.

Several forms of leucocytes are now recognized in inflammatory tissue, among them being the single and the polynucleated. The polynucleated are the type of the pus-corpuscle. They possess two or three nuclei or peculiarly deformed biscuit or sickle-shaped nuclei, which are supposed to be appearances which precede a breaking down of the cell (Fig 24). The single-nucleated cells are scarce in acute inflammation, but in the later stages and in chronic forms they are more common.

Many of the wandering cells derived from connective-tissue cells closely resemble the single-nucleated leucocytes, and cannot always be distinguished from them.

Regarding the origin of many of the cells seen in inflamed tissues, Grawitz has recently propounded a theory which closely resembles that already alluded to by Stricker. He claimed that the majority of these cells came from the intercellular substance. According to this theory, during embryonic development numerous cells change into intercellular substance and remain *slumbering*, as it were, in this condition until some irritation arouses them, when they return again to an active-cell type. This means that the fibrous tissue of connective tissue, the homogeneous tissue in cartilage, and the intercellular substance in bone are not excretory

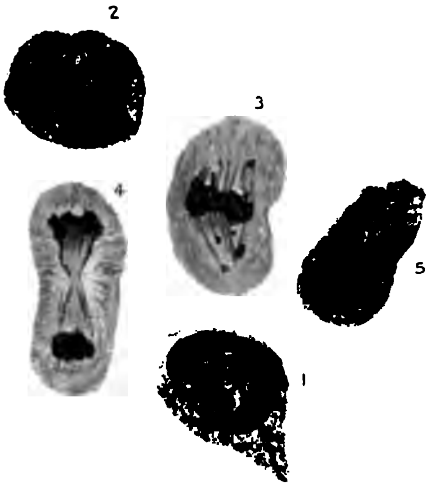

FIG. 26.—Karyokinesis in the Cells of a Sarcoma.

products of the cells, but that the bodies of the cells are actually changed into intercellular substance.

When these cells begin to appear the nuclei are extremely small and the cells seem to have no protoplasm. They are arranged in rows, and are so deeply situated in the bundles of fibres that one must conclude that they have originated *in loco* from their accustomed quiescent fibrous state, and cannot therefore have been transported thither by emigration. These cells are frequently seen in numbers when there is no sign of karyokinesis, indicating that the pre-existing cells of the tissue are not in an active state of development; which fact goes to show that they are not derived from other cells. The nuclei gradually enlarge, and acquire a cell-body that forms around the nucleus from the material of which the softening fibre is composed. When a considerable portion of the intercellular substance has changed to cell-protoplasm the fibre as such disappears, and it is replaced by a row of cells lying close to one another. These cells when once formed are precisely like those which existed before, and, like them, are capable of proliferation.

Shakespeare, whose work has already been alluded to, regards the flat or spindle-shaped cells seen in the primary bundles of fibres in the cornea, the cartilage, or the intima of vessels as cells which are usually invisible and which are not susceptible to staining processes. These cells, he thinks, are Grawitz's slumbering cells. Under the influence of irritation these cells are aroused to activity, and appear to acquire their original power both to destroy and to repair. Weigert vigorously opposes this idea of slumbering cells. The fibres, he says, are absorbed, being damaged or dead, and cells appear where they were before. The new cells come from the proliferation of the pre-existing cells. The absence of the signs of mitosis, or indirect cell-division, is no argument against their origin from the cells of the part, as this form of division is chiefly confined to cells that are intended as permanent cells.

What are the functions of the leucocytes? and why do they crowd in such numbers to the inflamed part? Cohnheim regarded them as the active agents in the process of repair, but according to Ziegler many of them are taken up by the proliferating connective-tissue cells, for which they appear to serve as nutriment. Many of these mobile cells appear to play the rôle of scavengers, owing to the power possessed by them of appropriating particles of foreign bodies or bacteria and transporting them to distant points. The usefulness of the leucocytes in consuming and receiving portions of the broken-down tissue can easily be understood, for there is here touched the principle of absorption, by means of which dead substances, blood-clots, and exudations are disposed of.

A new view of the function of these cells seen in inflamed tissue has been propounded by Metschnikoff, whose first studies on the action of the daphnia when attacked by the spores preying upon that organism formed the basis of his doctrine; which is, in brief, that the cells of the inflamed part and the invading organisms are opposed to one another in a struggle for existence. If the white corpuscles, or the *phagocytes*, are enabled to appropriate and to destroy the bacteria with which they come in contact, the system is protected from the germ; if, however, the bacteria are more powerful than the cells, a destructive local inflammation or a constitutional disease may result. Metschnikoff describes two kinds of phagocytes—the *microphagocyte* and the *macrophagocyte*. The former corresponds to the migrating leucocyte, and the latter are larger cells developed from the proliferated fixed connective-tissue corpuscles, which in some cases consume the smaller cells after their struggle with the bacteria, thus removing the débris of the inflammatory struggle and paving the way for an absorption of its products. In other cases they attack the bacteria directly: they are, for instance, more likely to take up bacilli, as in anthrax and leprosy. In tubercle the macrophagocytes figure as epithelioid cells and giant-cells containing bacilli, but these organisms are seen also in the leucocytes.

This doctrine is well illustrated by studies made by its author in erysipelas. He finds that in fatal cases of this disease only comparatively few leucocytes were seen, and none containing bacteria. In the cases recorded some of the cells contained a large number of the bacteria; other cells contained none. In some of the former there were perfectly-formed bacteria; in others the bacteria did not take the staining reagent so well, showing a degeneration of power; and in others granular débris only of bacteria was found. In gangrenous portions of erysipelatous tissue no cells containing bacteria were seen, the microbes all being free in the tissues.

Experiments made with the anthrax bacillus on animals not susceptible to this disease show well the action of the leucocytes, as this form of bacteria is so large that the organisms are studied with comparative ease.

In some diseases the macrophagocytes appear to be the active cells; in others the microphagocytes destroy the bacteria. Many observers have not accepted this doctrine, and they maintain that the loss of activity of the bacteria is either a spontaneous loss or one due to the antagonism of other forms of bacteria. Baumgarten points out that in relapsing fever the spirilli are not seen in the leucocytes, yet the patient recovers. The explanation of this is, probably, that the strife is not waged in this case in the blood, but in the tissues or the viscera, as the spleen. At all events, there is seen, in this doctrine, although it is as yet hardly removed from the stage of probability, a reasonable explanation of that condition known as *immunity*, by means of which certain animals are protected from certain diseases, and by which man is also protected from a second attack of certain diseases.

A word in conclusion regarding the action of the cells in inflammation. The number of cells found in an inflamed part is in proportion to the degree of inflammation existing there. If, on the one hand, the inflammation has been severe, the tissues will be found so filled with small round cells that it is difficult to recognize the original character of the tissue itself. If, on the other hand, the degree of irritation has been slight, as is often the case in wounds healing rapidly under aseptic treatment, a comparatively small increase in the number of cells of the part takes place.

Little has hitherto been said about the changes seen in the intercellular substance. In connective tissues this substance consists mainly of a network of fibres. In certain tissues, like cartilage or the cornea, this substance is more homogeneous in appearance, although with suitable reagents the fibrous nature is made apparent. Under the stimulus of inflammation there is great increase in the number of cells which more or less obscure the intercellular substance; but it is evident that a solvent action is exerted upon it, either by the cells that are present or by the fluid which is exuded from the blood-vessels, or by both. According to Stricker, the cellular substance returns to an embryonic state and becomes separated into particles of amœboid substances; in other words, it is broken up into cells again. According to most authorities, it is, however, simply melted down into a granular softened material, forming a matrix for the support of the vastly increased number of cells. When the cell-immigration is limited in extent there is seen but little change in the intercellular substance.

In addition to the escape of leucocytes from the blood-vessels, there is found a certain amount of fluid which has leaked through the vessel-walls into the inflamed part. This fluid is richer in albumin and is more concentrated than the serum exuded in passive hyperæmia, and it resembles closely the liquor sanguinis or blood-plasma. The fibrinogen it contains comes in contact with the fibrin-ferment and paraglobulin which are set free from the numerous breaking-down leucocytes, and fibrin is consequently formed. That this collection of fluid is not due to an obstruction of the capillaries can easily be demonstrated in a dog's leg by setting up an inflammation in the paw, exposing the lymph-vessel, and inserting a canula into it, when it will be seen that a considerable increase in the amount of lymph naturally exuded by the vessels is taking place. The coagulation of the lymph thus accumulated in the inflamed part gives to it a certain firmness which is characteristic. The product thus formed, with the cells which have emigrated from the blood-vessels, constitutes what is known as the *exudation.*

Such, then, are the changes which take place in the tissues during the origin and development of a simple or uncomplicated inflammation. The further progress of the inflammatory process will be considered in the succeeding chapter.

V. SIMPLE INFLAMMATION.

2. Symptoms and Causes of Inflammation.

Four cardinal *symptoms* of inflammation have from time immemorial been grouped together—namely, *rubor*, *tumor*, *dolor*, and *calor*, or redness, swelling, pain, and heat—to which modern writers have added a fifth, *functio læsa*, or disturbed function.

In a typical case of inflammation—as, for instance, an acute cellulitis of the arm of a powerful laboring-man—these symptoms are all apparent even to the most inexpert observer. The scarlet redness of the skin; the great distention of the subcutaneous tissue, forming a diffused and tense swelling, pressure upon which shows rapid changes of color, as the temporary bleaching of the part is followed by a hue deeper than before; the exclamation of pain which even careful handling elicits from the patient; the greatly increased warmth of the arm as compared with that of its fellow; together with the complete loss of power of the diseased limb,—all combine to form a characteristic picture of disease.

The rubor, or *redness*, is due to the increased determination of blood to the part. It differs from the color of hyperæmia principally in the variability of its hue. This change is partly due to varying rapidity of the blood-flow. When the congestion is at its height the color is scarlet, and the blood, when drawn by leeches or when allowed to flow from an incision, is of a bright arterial color, and it is more rapid than normal. The tint deepens as the current slackens, and as the blood-column, moving slower, loses more of its oxygen. In very severe forms of inflammation, when the swelling is excessive and the parts are unusually tense and the capillaries are crowded with red corpuscles, there may be an escape of red corpuscles with the leucocytes through the walls of the vessels, and in such cases they are usually collected together in little groups, forming what are known as *punctiform ecchymoses*. This is the explanation of the so-called "hemorrhagic" forms of inflammation, such as are seen in the eruptions of some of the severe types of exanthemata, as smallpox and measles.

Usually the color is brighter at the periphery of an inflammatory swelling, and deepens toward the centre, where the current is more impeded in its action. As the blood flows more slowly it has the more livid or bluish hue seen at the termination of an inflammation when it passes from the acute into the chronic stage. The presence of an abundant exudation diminishes the intensity of the color, as the blood-vessels are then surrounded by a more or less colorless fluid or a semi-solid mass. If firm pressure be made upon such a spot, the part will assume a somewhat yellowish tinge, due to the presence of the exudation. This appearance, which is characteristic in acute inflammations of the skin, enables one to distinguish between a genuine inflammation in its incipient stage and the temporary blush due to pressure or to stimulating dressings.

The color of an inflamed mucous membrane is much deeper than that of the skin, and is obviously due to the close proximity of the blood-vessels to the surface. The color is altogether absent, however, in bloodless parts, as in the cornea or the cartilage. In the latter cases, however, there is usually found congestion in the adjoining vascular tissues. A foreign body in the cornea will soon make its presence suspected by congestion of the vessels of the conjunctiva. The inflammation of the cartilage of a joint is accompanied by congestion of the vessels of the capsule of the joint, and sometimes even of the external integuments.

The tumor, or *swelling*, the second symptom, will now be considered. It might be supposed that swelling was due to the same cause which produced the redness—namely, increased flow of blood to the part—but in active hyperæmia there is no swelling, and in passive hyperæmia the swelling is due, not to the increased current of blood in the part, but to dropsical effusion.

If an incision is made into an inflamed organ, it will not only be found that more blood flows, but also that the tissues themselves are more juicy. If an inflamed mucous membrane is examined, there will be found, at certain stages, an increased and altered secretion. In an inflamed pleural cavity a clear or slightly opaque fluid, containing colorless coagula, is observed. Even irritation of the skin, as in burning, will show that here too more lymph is formed, which collects on the surface beneath the epidermis in the shape of blisters.

The exudation not only shows itself as altered secretion exuding from mucous membranes or as effusion into serous and synovial sacs, but a certain amount is retained also in the tissue itself, as in the capsule of the joint or in the mucous membrane of the throat, and produces swelling. The delicate areolar tissue of the eyelids or of the prepuce is often the seat of distention sufficiently great to cause alarm to the patient. Such tissues often swell when the seat of the inflammation is in an adjoining structure, such as the conjunctiva or the urethra. Dense organs when inflamed sometimes cause considerable collections of fluid in their vicinity. A portion of the "tumor" formed in "swelled testicle" is due to effusion into the tunica vaginalis. The great swelling of the soft parts of a thigh, when the subject of an acute osteomyelitis of the femur, is due to the excessive exudation into the areolar tissue. Such unusual collections of lymph, manifestly of a fluid character, accompanying severe inflammations, are known as *collateral œdema.*

Soft and spongy organs, when inflamed, however, become firmer. This fact is well illustrated by pneumonia, when the exudation, coagulating in the alveoli of the lung, gives it the consistency of the liver, the exudation being known as *hepatization.* Many of the forms of cellulitis are made manifest to the touch by the induration which the coagulated exudation produces. The outlines of such an inflammation are easily determined by gently holding the inflamed mass between the thumb and finger and moving it to and fro. The contrast with the surrounding flexible tissues is thus made apparent, and the "cake-like" hardening is a familiar condition, and a symptom often of value to the surgeon in diagnosis. A certain portion of such a swelling is possibly due to the proliferation of the cells of the part and to the formation of new vessels during the process of repair, but it is now known that much less swelling accompanies healing under strict aseptic conditions, and that the elements immediately involved in the reparative changes are not sufficiently bulky to cause an appreciable amount of swelling. This symptom in some cases may, indeed, be absent entirely, as in dense organs incapable of sudden changes or in organs so liberally supplied with lymphatics that the exudation may be absorbed almost as rapidly as it accumulates. Such is the case in many of the exanthematous inflammations of the skin.

As has already been seen, the exudation consists of an unusually large formation of lymph, a fluid of high specific gravity and containing a considerable quantity of albumin, and also an accumulation of leucocytes which have emigrated from the blood-vessels. This material, when poured into the meshes of a tissue or an organ, soon forms fibrin by coagulation, and imparts a certain hardness or induration to the inflamed tissue.

The cause of this symptom of inflammation has been the subject of much dispute. Why, under these circumstances, the blood-vessels should act so differently than in their normal condition is not easily explained. It is clear that there is greater permeability of the walls of the capillaries and small veins. This has been explained by assuming the formation of little holes or "stomata" between the endothelial cells lining these delicate tubes; and this hypothesis has the sanction still of some of the highest authorities. Cohnheim attributes alterations of function to molecular change in the wall, or, as Sanderson expressed it, there is a damaged condition of the vessel which causes it to leak. Landerer with much plausibility points out that there is more tension in the tissues supporting the capillaries than is usually supposed, as can easily be demonstrated by injecting fluids subcutaneously. It is found by experiment to be greater than in the veins and lymphatics. Clinically, the great distensibility of the fibres is seen also during the formation of an abscess, and their relaxation is observed after pus has been evacuated, as shown by the wrinkled appearance of the skin. It is by such support as this tissue gives that the integrity of the capillaries is preserved in health. The tissues, being relaxed by the inflammatory condition, permit the passage of the exudation through the walls of the vessels.

A sort of flooding of the tissues is produced by this process, and it is pretty generally agreed that this phenomenon has for its object the sweeping away of all injurious substances, whether chemical poisons, fragments of dead and injured tissue, or bacteria, and at the same time new materials are conveyed to facilitate the process of repair. The powers peculiar to the leucocytes or phagocytes when performing this duty, which enable them to act as scavengers and appropriate foreign particles and fragments of cells or tissue or injurious organisms of every kind, and the antiseptic properties of blood-serum, favor this view. The cures of many chronic diseased conditions by inducing an acute inflammation, the treatment of hydrocele by the injection of carbolic acid, or the obliteration of a chronic eczema by applications which produce a fresh inflammation, are all clinical illustrations of this protective influence of one of the apparently most alarming symptoms of inflammation. When, after an excessive inflammatory reaction, great swelling is followed by suppuration, it is seen that the old idea of a "peccant humor" rests on a scientific basis, and in the discharged contents of the abscess are found the remnants of the injurious substances which gave rise to the inflammation.

The *dolor*, or pain, is due to the pressure in the terminal branches of the nerves, and consequently it differs greatly according to the distensibility of the part or to the amount of exudation or to the nerve-supply. The inability of certain tissues to yield to the inflammatory swelling probably is the cause of the most severe pain. The suffering produced by an "ulcerated" tooth when deep-seated pus is endeavoring to reach the surface of the bone, and the pain from pressure caused by a felon, are sufficiently familiar examples.

Pain is usually most severe at the beginning of an inflammation, while the tissues are in process of being stretched, or when the exudation takes place so rapidly that the tissues have no opportunity to yield gradually. It is possible that there may in some cases be an undue sensitiveness of the nerves. Hyperæsthesia was observed by Claude Bernard in the ear of a rabbit after division of the cervical sympathetic.

The throbbing sensation which so often accompanies acute inflammation may be due to the extra pressure exerted by the arterioles during systole upon the sensitive nerve-fibrils. Boring pains are usually associated with chronic inflammations of bone, and are at times a source of great misery to the patient. Lancinating pains, which accompany more acute swellings, are suggestive of an abscess approaching the moment of breaking and discharging its contents.

Among some of the less severe forms of pain may be included soreness, generally characteristic of the furuncle. The soreness of a boil is proverbial. It means the formation of a small abscess-cavity in a yielding but superficially sensitive organ. It is proverbial also that itching is considered a good sign; which is undoubtedly true, for when pain ceases the inflammation is probably subsiding, and this symptom of itching is due to the infiltration of the parts about the terminal nerve-branches. The itching will not disappear until this residue of inflammatory products has been absorbed. Some portions of the body are much more sensitive than others. An inflammation seated at one of the outlets of the body where the skin and mucous membrane join is always productive of great suffering. Painful affections of certain organs are often referred to distant points. Pain in the uterus is felt in the back, but pain in the back, due to caries of the vertebra, is usually referred to the belly. In many cases of hip disease the pain is felt in the knee. Pain in the heel has been described as characteristic of a variety of diseases. It has been known to accompany inflammation of so distant an organ as the prostate gland.

Pain will often spread back along the course of a nerve, as if by sympathy, to adjacent branches. The pain of an inflamed finger may not only involve the fingers of the hand, but may spread also to the shoulder and side. The teeth likewise furnish familiar examples of such anastomoses of pain. Pain may altogether be wanting. This absence of pain is the case in some nerveless organs, also in grave inflammation when the severity of the inflammation endangers the vitality of the part.

The *calor*, or heat, is the last of the four cardinal symptoms. The increased warmth of an inflamed spot on the surface of the body is readily recognized by the hand of the surgeon, and a comparison with the corresponding spot on the other side of the body is thus easily made. The old-fashioned theory regarding this symptom undertook to explain this rise of temperature by assuming an increased chemical action in the part itself, by which action heat was produced, and that subsequently the superheated blood, being conveyed over the body, produced fever. But Hunter, who was the first to make thermometric observations on this point, came to the conclusion that a local inflammation was unable to raise the temperature of the part above that found at the source of the circulation.

Hunter's experiment, which has been quoted by many writers, was upon a patient on whom the operation for the radical cure of hydrocele had been performed. On opening the tunica vaginalis he placed a thermometer in the wound, and found the instrument registered 92°; the next day the mercury in the instrument, introduced as before, rose to 98¾°, being an increase of 6¾° in the twenty-four hours.

Recent investigators endeavored to show that the inflamed part produced heat. John Simon found with the thermo-electric needle, first, that "the arterial blood supplied to an inflamed limb was less warm than the focus of inflammation itself;" secondly, "that the venous blood returning from the inflamed limb, though less warm than the focus of inflammation, is warmer than the arterial blood supplied to the limb;" and, thirdly, "that the venous blood returning from an inflamed limb is warmer than the corresponding current on the opposite side of the body." These observations, which were put forward some twenty-five years ago, were later confirmed by C. O. Weber, an able German observer.

Claude Bernard, the distinguished French physiologist, found in his classical experiments on the ear of a rabbit after division of the cervical sympathetic, that the temperature of the ear became higher than that of the rectum, and Weber found that if the ear was irritated so as to produce a simultaneous inflammation the temperature would rise still higher.

As already seen, however—and, indeed, as the experiment just quoted proves—simple active hyperæmia of an external organ is always accompanied by a rise of temperature of the part, and this rise is due to the increased amount of warm blood which is carried there from the centre of the body. Observations on the temperature of the different tissues and organs show that the production of heat originates chiefly in the muscles, and to a slight extent also in the viscera; but, although much heat is manufactured near the surface, the more external portions of the body by exposure to a lower temperature and by evaporation are rendered cooler than the internal organs. Cohnheim has experimentally demonstrated that much more blood flows through the inflamed leg of a dog than through the sound leg, and concludes, therefore, that the rise of temperature is due solely to the increased amount of warm blood flowing through the part.

More perfect forms of thermo-electric apparatus have demonstrated also that although there is a considerable difference between an inflamed spot on the surface of an animal and the corresponding spot on the other side of the body, as shown by inserting thermo-electric needles into the symmetrical parts, yet the farther the inflamed spot is situated from the surface the less is the difference found in the temperature of the two sides. In internal inflammations, such as pleurisy or peritonitis, it was found that the temperature is no higher than that in the healthy pleura or in the peritoneum or in the heart of the animal experimented upon; and these experiments have been confirmed by similar observations taken in deep-seated inflammations in man.

The highest authorities have therefore concluded that the temperature of an inflamed part is in direct proportion to the amount of hyperæmia of the part. Recklinghausen thinks that it may be possible that a fractional part of the heat may be produced by chemical changes going on in the inflamed tissues or by increased oxidation due to a removal of nerve-influence, but there is yet no proof that any such local production of heat takes place. Modern observations have therefore been unable to disprove the truth of the doctrine which Hunter taught a century ago.

In inflammations of certain parts of the body it is obvious that this increased heat will be wanting, as in the lung or the kidney, and it is only in superficial tissues, whose temperature is habitually lower than that of the blood, that it is most marked. The process is analogous to that of a hot-water radiator: the greater the amount of water of a given temperature flowing through the pipe, the greater will be the amount of heat given off; the temperature of the radiator will never be quite so high as that of the boiler.

To the four cardinal symptoms of inflammation above described there has of late years been added a fifth, which, however, might equally well be regarded as a result rather than as a symptom of the inflammatory process. This fifth symptom is the *functio læsa*, or impaired function of the part.

It can easily be understood that a muscle which has been infiltrated with an inflammatory exudation, and which is hot, painful, and swollen, cannot act so readily as a healthy muscle. In such a case the muscle is found spasmodically contracted, and for the time being no relaxation of its tissue can take place. The sterno-cleido-mastoid muscle, which is often implicated in inflammations of the surrounding glands and cellular tissue, will sometimes cause considerable deformity by twisting the head, and the function of the muscle will not be restored until the inflammation has subsided. After fractures near joints there is seen great impairment of the motions of the joints, existing long after the bones have grown together, the tendons and capsules being more or less glued down and impaired in their natural movements by the exudation which has taken place around them and in the adjacent muscular tissue. Great dryness of the mouth accompanies inflammation of the parotids. The special senses are all impaired when the organs concerned in their function are inflamed: the eye cannot see, the nose cannot detect odors, and the ear cannot hear so well when inflamed as in health. Not only are the sensitive nerves pressed upon, but probably also those which conduct reflex actions, and likewise the motor and secretory nerves. The so-called "trophic" action of the nerves is sometimes so impaired that the nutrition of the organ is seriously affected, and atrophy or permanent degeneration of certain structures may take place.

As has been seen, each symptom of inflammation may be wanting at certain times. The redness will not be observed in nonvascular organs. The swelling will often be absent when the absorbents are sufficiently active to carry off quickly the exuded material, and there will be no material change in the temperature of the interior organs; but as the surgeon ordinarily sees inflammation—that is, in the external portions—these symptoms are almost invariably present in acute inflammations. In chronic inflammations—namely, in those which are not accompanied by such active pathological phenomena as have been studied, and which last a long time—none of the symptoms are so well marked as they are in the acute forms; many of the symptoms, such as heat, redness, and even pain, may altogether be wanting. There will always be found a certain amount of swelling or "thickening" of the part, or "induration."

Before attempting to define inflammation it is well to have an understanding as to the precise *seat of the process*. As been seen, the pathological changes are confined chiefly to the blood-vessels and to the tissues. Virchow, in advancing his theory of cellular pathology, maintained that inflammation could not be produced if the tissues were not directly irritated either from without or through the blood, and that the cells were thus enabled to attract inflammatory products through the blood, the phenomena of inflammation being thus produced. This was known as the *attraction* theory.

Cohnheim, whose studies on the action of the blood-vessels and the leucocytes have been quoted so often, regarded the wall of the smaller vessels as the seat of the lesion, and he assumed a molecular change in the vessel-wall to account for the series of changes which ensued, and which are distinctly different from those accompanying simple hyperæmia.

Neither of the above theories has been accepted in its entirety, as further observation has shown that the areolar tissue is so intimately connected with the smaller vessels that the two structures can hardly be considered separately from a physiological point of view; and it is difficult to conceive of a lesion affecting one without involving the other. Recklinghausen shows that the products of inflammation are so deep in the tissues and so little on the surface of membranes, but rather near the blood-vessels and the lymph-channels in the tissues, that the evidence is in favor of the view that the walls of the vessels and the surrounding tissues are the chief seats of inflammation. Different structures will of course be affected according to the route through which the inflammatory agent acts.

Most traumatic inflammations take their origin in the tissue, for they are directly acted upon by the knife, or in superficial injuries or contusions. The parenchymatous inflammations of the deeper organs—that is, the inflammations acting upon the cells which perform the special function of the organ—are examples also of this form.

Those inflammations which are conveyed through the blood affect those tissues which lie chiefly in the course of the vessels, and which, consequently, form the stroma or framework of organs, and are termed by the pathologist "interstitial." Typical examples of this form are seen in the kidney, the liver, and the brain from alcohol-poisoning, but the surgeon has also to deal with this class of inflammations in cases of acute infective disease.

Severe crushing injuries, strong chemical agents, or the effects of extreme heat and cold result in death of the part. Dead tissue frequently acts upon the surrounding tissues as a "foreign body," having become a source of infection. The agencies thus called into action exert themselves partly upon the tissues directly and partly on the vessels of the part.

What, then, is the *nature* of inflammation? The apparatus concerned in nutrition may, as has been seen, be so affected through the tissues or through the blood-vessels as to sustain an injury, or, as Sanderson expresses it, there occurs a "damage," which may result in death of the part, or, if acting less severely, may cause a series of changes such as has been described as characteristic of inflammation. It has, in fact, been pretty generally agreed that inflammation is a disturbance of the process of nutrition, and this view is expressed by Van Buren, who defines it as "a condition located in the apparatus of nutrition, affecting a limited area, and consisting in temporary perversion of nutrition from its natural and regular order." Observe that he does not regard it as a disease, but as a "condition," and "in the majority of cases not even a morbid condition." It is, in fact, difficult to determine exactly where a physiological process ends and a morbid condition begins. The condition of a muscle after excessive exercise is one which presents the symptoms of inflammation, although in a mild degree. It is swollen and warmer than natural, more blood circulates through it, and every one knows that it can also be painful. The dividing-line between such a state and true inflammation, between the physiological and the morbid process, is not a broad one. Sanderson, however, does not even regard it as a disorder of function, but as an arrest of function. The phenomena of inflammation are, he thinks, the signs of "damage." A damaged blood-vessel is relaxed for the same reason that a damaged heart or a damaged intestine is relaxed. The penetration of the leucocytes through the vascular wall is due, he says, to the power possessed by these amœboid bodies to introduce their own substance into that of dead tissue or into any material capable of imbibition with which they are brought in contact. These views are not at all in harmony with those held a generation ago, when inflammation was regarded as an increased nutrition of the part. This nutrition was supposed to be necessary to enable the tissues to repair the injury to which they had been subjected. Before the days of antiseptic surgery it was thought that a brisk inflammation was essential to seal the lips of a wound, but it is now known that union can take place with hardly a sign of inflammation. Repair need not, now-a-days, be looked upon as part of inflammation, but, as Sanderson says, as the result of the power of renewal in the adjacent undestroyed tissue. These facts are becoming more evident as year by year the surgeon becomes convinced of the difference between the old "traumatic inflammation" and the uncomplicated process of repair.

Inflammation cannot, however, be regarded as simply an arrest of function. The apparatus of nutrition still continues to perform its duties so long as its vitality is maintained, although in an imperfect way. Moreover, we have to deal here not only with the nutrition, but with the protection, of the part affected. The new cells are present, not only for the purpose of repair, but also to ward off or to remove injurious particles and poisons. In attempting, then, to describe the nature of inflammation it should, in the light of the latest discoveries, be defined as *a lesion in the mechanism of nutrition, owing to which its efficiency is impaired, but which, if not so severe as to cause death, produces conditions favorable for the protection and repair of the part.*

The leakage of the vessels causes an increased formation of lymph, which flushes and washes out the morbid tissues, exerts an antiseptic action, and brings with it the protecting phagocytes and the materials suitable for repair.

Inflammation has been likened to a conflagration which destroys without repairing; but the forest fire, although it carries destruction in its path, sweeps away also the pests that prey upon vegetable life, and leaves behind in the ashes materials and conditions suitable for a new growth of timber.

Inflammations arise from manifold *causes*, but they have usually been classified into three separate categories: (1) trauma or mechanical injury; (2) chemical action, including usually heat and cold and drugs, and, by some authors, also the poison of insects and serpents; and (3) infection, due to the action upon the tissues of micro-organisms known as *bacteria*. There are other agencies that cannot well be included under any of these heads, such as the action of the nerves, about which there has been much dispute, and the exclusion of blood from a part for a certain length of time. This, as has been pointed out, can be done experimentally by the application of a rubber ligature to the ear of the rabbit or to the tongue of the frog; but there are also clinical examples of it in the inflammation which precedes a bed-sore or in that which follows the milder forms of frost-bite. The action of heat brings about distinct chemical changes in the tissues, and it should not therefore be associated with cold as a similar cause of inflammation, as is ordinarily done.

Examples of inflammation due purely to trauma are seen in extensive contusions and simple fractures. In such cases bacterial action may, in the great majority of cases, be excluded, and yet in a simple fracture of the tibia, for instance, the symptoms of inflammation are seen well marked. The whole region from the ankle to the knee-joint is swollen, hot, and painful, and the limb is rendered useless. The color varies according to the amount of exudation and hemorrhage which occurs in the tissues. It is not, however, a brilliant red, such as is seen in infective inflammations. Such inflammations do not have a tendency to spread.

Examples of *chemical action* are furnished by drugs which may have a predilection for certain organs, where they will produce inflammation if used in poisonous doses. Thus, mercury will act upon the mouth, producing salivation, and cantharides upon the urinary organs; gouty inflammations may also be placed in this category.

The group of purely toxic inflammations are most appropriately placed under the head of chemical action, for such is the nature of the poison of serpents and insects, so far as known at the present time. There are also chemical substances developed as the result of bacterial action, but these are incidental features of infection, and cannot be classed in the former category without much confusion. To this class of substances belong the ptomaïnes. The poisonous action of certain plants, such as ivy, is another example also of the group of chemical poisons.

The action of *bacteria* in producing inflammation is now recognized everywhere. The relation of these micro-organisms to the inflammatory process will be considered in another chapter. The prominence which should be ascribed to them as causes of different kinds of inflammation is a question about which there has been, and is still, considerable difference of opinion. As progress is made in the minuter knowledge of the germ-theory of disease there is a tendency to relegate to the action of bacterial influence a larger and larger number of inflammations. Extremists, like Heuter, maintained that all inflammations were due to bacteria. Sanderson quotes him as follows: "Septic organisms exist everywhere, ready, whenever access is offered to them, to enter the body and fulfil their morbific function. Consequently, inflammation may be defined, with reference to the universality of its cause, as an epidemic and contagious disease which prevails universally over the whole world, with the exception of mountainous regions near and above the line of perpetual snow. Here there are no germs, and, we may presume, no possibility of inflammation."

Heuter's views were based upon the experiments of Zahn and others that subcutaneous tissue could be destroyed by the actual cautery or by chloride of zinc without causing inflammation. These experiments will be discussed elsewhere.

It was well that Lister raised a warning voice against the tendency of the time, and at the Congress in London he undertook to show that the germ-theory of inflammation was carried too far, and illustrated his point by showing the influence which the *nervous system* has upon inflammation. If the nerves take no part in inflammation, of what use, he argues, is counter-irritation, such as the actual cautery in joint disease or the treatment of sore throat by the use of mustard? If this kind of treatment cures an inflammation by withdrawing nerve-action from the part, it follows that the disease was maintained by an abnormal action of the nerves. Catching cold is thus defined by Lister: "A diminution of the action of the nerves of a part of the surface, leading to the increased action of the nerves of an internal organ in sympathy with that part." Vañ Buren, however, explains catching cold by an arrest of function of the skin as an emunctory, whereby certain effects and presumably noxious materials which should be eliminated are retained and act as blood-poisons. This view of an auto-infection, which is gaining ground, has lately been brought forward to explain many febrile and inflammatory disturbances due to ptomaïne absorptions arising from gastric and intestinal disorders.

The influence of the nerves has long been recognized as an agent active both in the nutrition of the part and in producing inflammation. The theory of the *trophic* action of nerves was based largely upon the classical experiments on the vagus and trigeminus. After division of the ophthalmic branch of the fifth pair of nerves a necrosis of the cornea occurs within a short time, which condition eventually leads to destruction of the eye. The so-called "vagus pneumonia" is an inflammation of the lungs following division of the nerve. But these experiments have been explained in other ways. The division of the trigeminus was found to interfere with the power of winking and with the secretion of tears, and the insensibility of the cornea permitted abrasions and ulcerations which opened the way for an invasion of bacteria. Careful protection of the eye by stitching the lids together prevented inflammations. Vagus pneumonia was found to be caused by anæsthesia of the larynx and paralysis of the œsophagus, which allowed the saliva and food to flow into the bronchial tubes. The so-called "schluck-pneumonie" of the Germans corresponds to this, and it is occasionally a sequel of severe operations upon the tongue and throat. In such cases as this there is also an extensive infection of the lung with bacteria.

Such explanations as the above have served to throw considerable doubt over the influence of the trophic nerves, or indeed as to their very existence, but Graefe has shown that if the trigeminus is left uninjured, but an equivalent of exposure of the eye is produced by cutting away the lids and the lachrymal gland, there is not nearly so much inflammation as there is upon section of the nerve, and it is also of a different kind. Moreover, cases every now and then occur which are strongly suggestive of nerve-action. Of such was a case of left pleuro-pneumonia with herpes of the lower side of the chest. Vernet reports a case of acute right lobar pneumonia, with herpes of the palate, throat, and nose and over the right eighth intercostal nerve and the last phalanx of the middle finger of the right hand. Naso-labial herpes on the same side as the lung lesion has frequently been noticed. Herpes zoster is an example of a pustular eruption following the course of a nerve, and is accompanied with infiltration of leucocytes both around the terminal branches and the trunk of the nerve.

A gentleman eighty years of age was exposed to the draught of an open window while riding in the cars—an unusual exertion for him to make. Two days later herpes zoster of the occipital region of the exposed side came on and ran a typical course.

Paget in his lectures has described examples of the effects which disturbance of the nervous force may produce on the nutrition of a part. Inflammation of the conjunctiva may be excited by stimulus of the retina. Impairment of the nutrition of the skin as a result of injury of the nerves is sometimes manifested by a peculiar glossy condition of the integument. The vaso-motor disturbance described by Mitchell, Morehouse, and Keen has already been studied in a previous chapter. Swelling and inflammation of the finger-joints have been observed after fracture of the internal condyle of the humerus, causing an irritation to the ulnar nerve, and they have also been observed after Colles's fracture.

The condition of the bladder after the destruction of the spinal cord has long been ascribed to removal of the protective influence of innervation. Many of the cases of urethral fever which were supposed to be typical examples of reflex inflammation are now well known to be due to bacterial infection, but a certain number of them are difficult to account for in this way.

A man of middle age, with secondary syphilis and a stricture of large calibre of the pendulous urethra and two perineal fistulæ, entered the Massachusetts General Hospital for treatment. The first day an attempt was made to pass a polished steel sound of about No. 12 calibre, but, although the stricture did not yield, not enough force was used to draw blood, and the attempt, which was quite painful, was abandoned. On the second day there was high fever with suppression of the urine, and death occurred on the third day. At the autopsy the kidneys were found deeply congested and an acute nephritis existed.

Norton defines urethral fever as "a reflex paralysis, or, in other words, an exciting impression upon or injury to a set of peripheral nerves which by reflection through a centre may result in paralysis of the whole or a part of the united cerebro-spinal and sympathetic-nervous system, ... bringing about structural changes or suppuration in organs or other tissues."

Norton reports a case of sounding for stone in oxaluria, after which there were fever, rigors, partial right hemiplegia, and ptosis of the left side, and hyperæmia of the left side of the neck and face. Five weeks later an effusion into the left tunica vaginalis occurred. In a second case—one of stricture—catheterism produced high fever, later suppression of urine, and later still herpes of the face and neck. The writer assumes an "arterial fluxion" of the testis and kidney in these cases.

Suppuration, Norton thinks, may occur in these organs, and abscesses in distant parts may even occur, solely from reflex irritation.

Börner describes nervous swellings, of considerable dimension, of the skin accompanying menstruation and the menopause. These swellings were seen about the face and the lips, and also in other parts of the body, and they consisted of an active hyperæmia and also of a considerable exudation of lymph—a condition closely allied to inflammation.

Although the writer is not prepared to follow these observers to the full extent of their theories, yet it must be acknowledged, from the large mass of accumulated information showing such a close relation between nerve-action and inflammation, that it seems reasonable to assume that the old views are not entirely without foundation. It may be, in some cases, that the innervation of the part is so affected that bacterial invasion can take place, which would have been successfully resisted by the tissues in health.

Foreign bodies produce suppuration by means of bacterial action. They may undergo decomposition, or, if composed of a substance not capable of decomposition, they may excite a local irritation which favors bacterial infection of the surrounding parts.

Among the predisposing causes of inflammation may be mentioned that of *age*. Disturbances of nutrition in growing children lead readily to inflammations which are not likely to occur in the adult, such as affections of the mucous membranes and of the bones. In old age the power of resistance to invading organisms is less marked, and many catarrhal affections are seen at this period. Morbid conditions of the blood (such as gout, scurvy, diabetes mellitus) subject the patient to inflammations of the joints, of the mucous membranes, and of the skin. The influence of climate is also a potent factor both in wintry and in changeable climates, like that of New England, where affections of the throat and of the œsophagus, and, in more equable and tropical countries, where the abdominal viscera are more liable to inflammations. The habits and customs, and even the costumes, of nations are affected by these influences; the scarf or muffler of the Northerner is replaced by the belt and sash of the inhabitants of the East.

3. Varieties and Treatment of Inflammation.

Formerly it was customary to divide inflammations into two general *varieties—idiopathic* and *traumatic*. The latter variety included those inflammations arising from injury of whatever kind; the former variety embraced those inflammations which were supposed to arise spontaneously. Little was known about the etiology of inflammation at the time this classification was made, but as the knowledge of pathological processes has increased less is heard of idiopathic inflammations, the term being now rarely used, and only in a limited sense to indicate inflammations that are not traumatic. The form of inflammation to which the present studies have hitherto been confined is the *simple* inflammation—that is, the *non-infective* form of inflammation. The causes of such an inflammation, as has just been seen, may be various, but there are no complications such as would be accounted for by the presence of bacteria. Burdon Sanderson says of it: "An uncomplicated inflammation is neither reproductive nor infectious, neither benign nor malignant. It has no tendency except the tendency to leave off as the occasion for it ceases." *Infective* inflammations are those due to the presence of bacteria, and they are in marked contrast to the form just mentioned. They are destructive in their nature, and through the action of those organisms the inflammation spreads progressively until whole organs are destroyed.

The division of inflammation into *sthenic* and *asthenic* is based upon the condition of the soil in which the disease occurs, rather than upon the nature of the process itself. A sthenic inflammation is one in which all the phenomena are present and well marked in character, such as is likely to occur in previously healthy tissues and in a powerful and vigorous subject. The color of the inflamed focus is a brilliant scarlet, the swelling is pronounced. and the part is hot and highly sensitive to the touch. The disease runs an acute course, whatever may be its termination.

Asthenic inflammations occur in old or in feeble individuals, and are marked by symptoms so slight as frequently to be overlooked. They play a conspicuous part in many of the complications which attend disease and injuries in the aged. Hypostatic inflammations, which are familiar to the surgeon as the result of a feeble circulation, occur in dependent portions of the body during prolonged confinement to the bed. Such is the occurrence also in old people of pneumonia during convalescence from an injury or an operation. A very slight cause may in these cases be sufficient to give rise to a condition which may become more grave than the original lesion. The terms "sthenic" and "asthenic," however, are rarely used.

An anatomical division of inflammations may be made if we choose, with Virchow, to classify them according to the seat of the tissues attacked.

According to this view, *parenchymatous* inflammations are attended by the changes seen in the cells peculiar to a given organ, which cells become cloudy from granules deposited in their protoplasm, and subsequently undergo degenerative changes, and, if on the surface, they are thrown off by a process of desquamation. These changes are, however, at the present time regarded as degenerative from the beginning, as the term "parenchymatous" is no longer considered as representing a special type of inflammation.

Interstitial inflammations involve the parts around the blood-vessels, and consequently they occupy the connective tissue forming the stroma of organs. They are usually chronic in course, and are attended with the formation of cicatricial tissue, which contracts and is attended with a gradual diminution in the size of the organ—a condition known as *cirrhosis*.

Inflammations can be divided into various classes according to the prominence of certain pathological conditions. In some cases it is found that there is an unusually small number of white corpuscles in the serum, and this fluid may contain less albumin than usual. This form is called "serous" inflammation, a familiar example being the abundant effusion sometimes attending a mild form of inflammation of the knee-joint. Many of these so-called "dropsies" of the joints are undoubtedly the result, simply, of an altered function of the endothelial cells lining the synovial membrane, but others are the outcome also of a genuine pathological condition, such as an inflammation following injury or some constitutional condition, as rheumatism. The abundant collections of fluid deposited in loose tissues in the neighborhood of acute inflammations, as in the eyelids or in the prepuce, are of the same serous character, and are the result of pressure which has forced the serum in the direction of least resistance. The fluid will in this case be thin and watery, having already been deprived of its fibrinogen while in contact with the leucocytes. These collections of serum may in some cases become an element of danger, as in extensive inflammatory swellings of the neck, where there may be pressure upon the laryngeal nerves or an œdema of the larynx which may seriously obstruct respiration. The amount of serum—or, more correctly, of liquor sanguinis—which exudes from the vessels when the surface of the wound has been irritated is much greater than one might suppose. These collections of fluid may become a great obstacle to the process of repair by forcing apart the lips of a wound, and it has been the object of no small amount of study on the part of surgeons to devise some means to provide for this excess of exudation.

When a large number of leucocytes are present, and when, owing to the severity of the inflammation, there is considerable disintegration of these corpuscles, possibly the result of a struggle with certain forms of bacteria, coagulation of fibrin takes place, and the exudation, if it be liberated into the interstices of areolar tissue, solidifies. If the exudation takes place upon a mucous surface, a pseudo-membrane is formed by the fibres of fibrin interlacing with one another and enclosing leucocytes in their meshes. Such *fibrinous* forms of inflammation may be the starting-point of organized tissue, and later blood-vessels may shoot out into these membranes, new tissue being thus developed. In this way two opposing surfaces, as in the peritoneal cavity, may be glued together, and the new-formed tissue is known as an *adhesion*. Here, again, the protective influence shows itself, for in this way perforations of the intestinal canal may be closed and the peritoneal cavity may be shut off from an invasion of bacteria, which abound in intestinal secretions. Certain serous membranes are particularly prone to such adhesive forms of inflammation, and the adhesions which form may impair the motions of the opposing surface, as in the pleural cavity or in joints, and may thus constitute a more or less serious complication. It is due to the adhesive nature of lymph that the edges of a wound are quickly sealed together. This complication rarely occurs in mucous membranes; for the epithelium, so long as it is preserved, prevents the formation of fibrin, and there takes place a serous discharge holding more or less leucocytes and some epithelium in suspension, and constituting the condition known as *catarrh*. In severer varieties of inflammation coagulation of the fibrin takes place, and a membrane is formed upon the surface which is known as *croupous*. There is no tendency to organization nor to the formation of adhesions in these cases, for the presence of bacteria brings on a discharge of a mucous or purulent character which sweeps away the membrane thus formed. A *diphtheritic* membrane is formed by a hyaline transformation or coagulation-necrosis of the tissues composing the mucous surface itself.

This change in the tissues is due to the presence of bacteria, and it is probable that the tendency of the fluids of the tissues to coagulate, and the tissues themselves to be transformed into a more or less homogeneous material, is due to the action of some substance liberated by these organisms during their development and growth. Such a mass of dead tissue—which if it occurred in a wound would be called a "slough"—can only be separated from the living tissues by a process of liquefaction, this change being effected through the medium of *suppuration.* When pus is formed, the fibrin cannot coagulate, or, if already coagulated it will subsequently be dissolved, owing to the presence of a chemical substance known as *peptone*, or some substance formed by the bacteria of suppuration having a solvent action.

When suppuration takes place the croupous or the diphtheritic membranes are separated and are carried off, and in their place is found a formation of pus covering an ulcerated surface, which by subsequent cicatrization may heal and return to a normal condition. Pus may, however, be discharged from an inflamed mucous membrane whose epithelium has not been destroyed. Such is the nature of the gonorrhœal discharge, consisting of plasma filled with innumerable leucocytes, forming a creamy fluid in which there is no tendency to coagulation owing to the presence of the gonococcus.

Hemorrhagic inflammations may be mentioned again in this place, merely to state that they are due to a high grade of inflammation resulting in an intense congestion and stasis in the capillaries. Red corpuscles are thus forced out by pressure. But the same conditions may be brought about by weakness of the vessel-wall as the result of a hemorrhagic diathesis or in connection with new formations where the tissues have a feeble organization, as in cancer. The existence of blood in the exuded serum or lymph is characteristic of certain affections. In the hernial sac a bloody serum accompanies strangulation of the bowel, being partly due to passive hyperæmia and partly as the result of an inflammatory congestion of the peritoneum. The aspiration of bloody fluid from the pleural cavity is a symptom strongly suggestive of the existence of malignant or tubercular disease.

Inflammation may terminate either in resolution, in death of the part, or in suppuration. A termination by resolution means that the various symptoms gradually subside and disappear and the part returns to its normal condition. When the inflammatory agent ceases to act, the distention of the vessels begins to subside and the flow of blood to resume its natural course. The heat and increased redness therefore begin to disappear from the part. The rapidity with which the swelling goes down depends upon the amount and the character of the exudation which has taken place. If this exudation has been largely serous, containing but few corpuscles, the lymphatics will be able to take it up speedily and effectually. If, however, a larger number of leucocytes are present, it will not be possible for the lymph-channels to provide rapid absorption from the inflamed area. Some of these cells are taken up by the lymphatics and carried back into the circulation; some undergo degenerative changes; others have already broken down during the progress of the inflammation, and their substance appropriated by larger cells, the "macrophagocytes." In this way the débris of the inflammatory process is swept away.

If, however, the exudation goes on to such an extent that the part is completely infiltrated with leucocytes, the structure of the tissue itself will seriously be impaired, for, as the leucocytes accumulate in large numbers, the fibres and the cells of the part disappear. The fixed cells undergo proliferation and become indistinguishable from the migratory cells, and the intercellular substance is gradually changed into a more or less homogeneous granular material in which the new cells are imbedded. The tissue thus formed, which is a temporary tissue of an embryonic character, replaces more or less completely the normal tissue of the part, and constitutes what is termed *granulation tissue.* Under these circumstances not only must absorption of the new cells take place, but a considerable reparative change must occur before the parts can return to their original condition. An inflammation which terminates by resolution is usually of a milder type.

In some forms of inflammation all the symptoms may be much severer, particularly the swelling. This swelling may occur to such an extent as seriously to impede the flow of blood to the part, and stasis or a stoppage of the flow of blood through the muscles will take place. Should this swelling be limited only to a small area, such as is supplied by a few capillary vessels, probably no permanent ill effects would follow, but more extensive obstruction to the blood-flow would undoubtedly lead to death of the part. Such complications, fortunately, are rare, but they are sometimes seen following inflammation of the mouth in children, and they involve a slough of an extensive portion of the cheek, as in noma. They are, however, usually secondary to other diseases, and belong chiefly to the class of infective inflammations. When mortification of a considerable portion of a limb follows a traumatic inflammation, it is generally found that some complication has occurred, such as the rupture of an artery. Another and more frequent termination of inflammation is suppuration, but this branch of the subject will be considered in another chapter.

In studying the *treatment* of inflammation it is well to consider whether there are any therapeutic means which, in the light of the present studies, will enable the surgeon to produce an effect upon the local processes.

In former times the belief was strong that such an effect could be produced, and for this purpose all the measures which belonged to what was then known as the *antiphlogistic treatment* were brought to bear. These measures consisted not only in local remedies, but also in such remedies as powerfully affected the whole system. Venesection was not infrequently accompanied by an emetic. It was thought that by abstracting blood and thus weakening the heart's action less blood would be carried to the part and the violence of the process would be subdued. Leeches, blisters, heat, and cold were alternately applied to the part with the view of directly combating the processes themselves, without taking into account the causes which produced them. The exudation, it is true, was supposed to be due to a fibrinous crasis, and mercury was also freely used to exert a solvent action upon the coagulated lymph, thus favoring absorption.

The antiphlogistic has now given way to the antiseptic treatment; that is, therapeutic measures are now directed rather against the causes than the result of inflammation. The treatment of to-day is mainly directed to prevention of inflammation, and how far this attempt has succeeded few are able to realize who are unfamiliar with the appearance of hospital wards before the antiseptic era. Still, inflammation is always present in a more or less aggravated form, and appropriate remedies are as much in demand as ever. Attempts have been made to determine whether an intimate knowledge of the processes of inflammation enables one to combat them scientifically. The treatment of the septic forms of inflammation or those due to bacteria will be discussed in another place. The point more especially of interest now is to determine the degree of influence which remedies will exert upon the processes themselves. Nancrede, who has studied this question experimentally, points out that in inflammation the excess of plasma cannot be carried off by the lymphatics, as they are compressed by the swelling of the parts and are blocked with leucocytes. The vessels are distended, and the existing intravascular pressure favors an excess of exudation, which is aggravated also by the presence of unusual numbers of red corpuscles that bring an excess of oxygen to the part, thus exciting the leucocytes to increased amœboid action and to their consequent migration.

A theoretically-perfect remedy should therefore relieve pressure from the heart's action, thus preventing over-distention of the already distended blood-vessel's walls. It must prevent also such ingress of blood as to cause an excess of oxygen with the increased exudation that results, and it must favor the escape of blood on the venous side, so as to drain off the stagnant blood. The heart's action, though diminished in force, should be increased in frequency to favor a return to active circulation.

Nancrede divided a large vein on the distal side of the circulation in the inflamed tongue of a frog. "The effect," he says, "upon the obstructed vessels was first an oscillation of the blood-disks, then an occasional momentary flow of blood, then suddenly a rapid resumption of the circulation, sweeping out the blood-vessels and apparently restoring them to their normal condition, except at spots where the agents inducing the inflammation had chemically destroyed the vessels or coagulated their contents."

Gensmer produced a more decided effect upon the circulation in the web of a frog's foot by applying a leech to the hock-joint. General bloodletting by opening an abdominal vein was inferior to leeching near the affected area. Local bleeding, Gensmer thinks, relieves stasis and causes a more abundant supply of arterial blood to the part, thus better nourishing the tissues, and enabling them to withstand the effect of the inflammatory process. He says the water is increased and the oxygen-carriers are diminished in the blood-vessels of the part; the action of the heart becomes more rapid and its force lessens. Here, then, is secured the desired effect upon the circulation.

Arterial sedatives were not found to have the same effect upon the circulation. Experiments show that, in giving gelsemium, the arteries become smaller, that the current is slower, and that stagnation is increased. Nancrede concludes that during the stage of active hyperæmia little danger exists of changes in the walls of the capillaries and of exudation. At this stage ergot or arterial sedatives would act favorably by reducing the size and rapidity of the current, thus allowing the veins of the irritated area to empty themselves, and giving the circulation an opportunity to return to its normal condition.

After the stage of capillary stasis is reached arterial sedatives can only do harm, and blood should now be removed from the venous side of the circulation. The best results are obtained by bleeding from one of the principal veins leading from the inflamed focus. When bleeding is impossible leeching or wet cups should be resorted to. In this way the vessels are not only emptied, lessening the pressure, but an aspiration is also invoked which increases the rapidity of the flow, and this flow, as it is unaccompanied by increased pressure, sweeps away the leucocytes and removes the excess of oxygen, and thus lessens migration ; it also helps absorption of the exposed lymph. This absorption occurs a few hours after the leeching, as shown in the wrinkling of the skin seen about that time.

In the later stages of inflammation arterial sedatives act favorably after bloodletting, because they lessen intravascular pressure, thus permitting the vessels to recover their normal condition. By lessening the bulk of blood in the part sedatives relieve nerve-pressure and, consequently, pain. Independently of bloodletting, they would act favorably only on the surrounding congestion, and would not help the conditions obtaining in the inflamed focus itself.

Such studies as these, which have more than a theoretical value, should be encouraged, for they are of great service in helping one to obtain an intelligent idea of how to attempt to control the circulation in deep-seated inflammation, particularly in the brain, where slight changes in the current of blood within the vessels or of exudation into the delicate tissues surrounding them are productive of grave results.

As local applications to inflamed parts both heat and cold act favorably by the action they produce upon the blood-vessels. The ice-bag can be applied in those cases in which congestion of vessels is a prominent feature, and where redness and heat are consequently pronounced symptoms. The soothing action of cold always makes it a welcome application. If, however, the swelling is great, the circulation is sluggish, the color is dusky, and the temperature of the parts is low, cold would tend to aggravate rather than relieve the symptoms.

Heat acts differently according to the degree used. Warm poultices favor an increase of hyperæmia and consequent flushing of the part. The exudation may thus be increased until pus forms, or the flushing of the part with blood-serum may bring about an antiseptic action, and thus prevent suppuration. Heat will in this way favor the absorption of the exudation, and it will in any case have a soothing influence upon the nerves of the part. Greater heat will constrict the blood-vessels. Thus very hot poultices, frequently applied, will sometimes check an incipient inflammation, and in chronic congestion of the cervix uteri the hot douche exerts its curative influence by this action upon the vessels.

The influence of counter-irritation has already been alluded to. Counter-irritation can be applied either in the shape of the actual cautery or the blister or in milder ways. It alters in some way the nerve-action of the part, and thus controls the circulation. It exerts its influence partly by reflex nerve-action and partly upon the local vaso-motor apparatus. It also stimulates absorption. Internally opium may be given to relieve pain and to ensure rest to the part. As a rule, depletive measures should be avoided, and the strength of the patient should be maintained by careful attention to his diet and to his surroundings.

VI. INFECTIVE INFLAMMATION.

1. Etiology.

Thus far, attention has chiefly been called to the simple forms of inflammation. The form that will next be studied has the peculiar characteristic that its tendency is not, like that of simple inflammation, to remain local and to subside, but rather is to spread and involve surrounding parts. *This peculiarity, which renders it a much more formidable type of disease, is due to the presence of bacteria.* The surgical affections caused by these organisms may be considered as complications attacking the healing of wounds, and constitute that group of affections known as the *traumatic infective diseases.*

Infective inflammation terminates, in the great majority of cases, in suppuration, and the forms of bacteria now recognized as the cause of pus-formation are known as the *pyogenic cocci.* Infective inflammation differs, therefore, from simple inflammation in its bacterial origin and in the destruction of tissue which it involves. The old view of suppurative inflammation, as described by Billroth and elaborated by Cohnheim, was that it consisted in an enormous multiplication of the cells of the part due to diapedesis of leucocytes, and that the fluid portion of the exudation failed to coagulate, and that this, with a softening of the intercellular substance, produced liquefaction of the tissues, thus forming pus. Why the fibrinogen did not coagulate was not precisely understood, but it is now known that fibrinogen is changed by the bacteria into *peptone.* This peptonizing action of the pyogenic cocci is one of their most marked peculiarities, and the fermentation which occurs in the products of suppurative inflammation is thus adequately explained.

The *frequency* with which these organisms are found in the human subject is pointed out by Ogston, who examined the pus from one hundred abscesses. Cocci were found in all *acute* abscesses, and were absent in all *cold* abscesses. The experience of subsequent observers has practically been the same. The only points about which there is at present any question are the etiology of the cold abscess and the relative frequency with which the different types of pyogenic cocci are found in the different clinical varieties of acute suppuration. It was at one time supposed that the cold abscess was caused by the bacillus of tubercle only, but this view has not fully been sustained. In a large number of cases it is not possible to demonstrate their presence either in the contents or in the walls of an abscess. The absence of pyogenic cocci, as shown by the failure to obtain a culture from the pus of a cold abscess, is explained by the dying out, owing to their age, of the organisms concerned in the abscess. This explanation does not seem to be altogether satisfactory, inasmuch as the *cultures* of these organisms show that they can retain their vitality for a very great length of time. It is possible that cocci may settle and form a deposit at the bottom of an abscess, the other portion of the pus being sterile. Ogston has demonstrated that the numbers of cocci greatly vary according to the activity of the suppuration. In acute abscesses he found an average of 917,775 cocci to 1 c.mm. of pus, and in the more chronic forms of abscess there were only 395,500 cocci. The fact is, that cocci are found in many of the abscesses originally starting from tuberculosis of the bone. H. C. Ernst demonstrated the presence of the aureus, albus, and tenuis in several cases of psoas abscess. Rosenbach obtained general tuberculosis in animals by injecting pus from cold abscesses, and the cultures taken from the same pus proved sterile.

The types of disease in which pyogenic cocci are found are acute localized abscesses of all kinds, such as boils, carbuncles, suppurating glands, empyema, abscesses of the parotid, mamma, and tonsil, synovitis, and osteomyelitis. In these forms the staphylococcus group is usually found. The streptococci are more frequently seen in the spreading inflammations, such as phlegmonous cellulitis and phelgmonous erysipelas.

Experiments on animals have abundantly proved that cultures of these organisms when injected into their tissues would produce suppuration. One or two examples it may be well to give.

Knapp tested the action of sterilized foreign bodies when introduced into the cornea, and found that suppuration did not take place, but when the object was previously dipped in a pure staphylococcus culture suppurative keratitis always occurred. H. C. Ernst injected into a guinea-pig the staphylococcus pyogenes aureus from a perinephritic abscess which occurred in a patient in the writer's hospital service, the patient subsequently dying of pyæmia. The seventeenth generation was used for the purpose, the culture process lasting over a year. There was developed in the guinea-pig an abscess full of thin yellow pus, cultivations from which showed the presence of the staphylococcus aureus.

It has been proved, however, that under certain circumstances injections of the pyogenic bacteria will not produce suppuration. The experiments of Gram on the peritoneal cavity of animals has a bearing upon this point. He found that a considerable number of bacteria could be introduced into the peritoneal cavity without affecting the health of the animal. He concludes that in order to act the pyogenic cocci must have certain conditions of the tissues pre-existing that germination may take place. So long as the surface of the peritoneum remains uninjured, millions of bacteria may be absorbed, but if fluid containing them is injected in such quantity that it cannot be absorbed readily, or if the peritoneum is injured, peritonitis will occur.

Rapidity of absorption will equally well save other parts of the body from the ravages of the pus cocci. This has repeatedly been proved to be the case after the injection of pure cultures into the subcutaneous tissue of animals when the point of injection has been touched by the actual cautery. The heat acted as a stimulant to the absorbents, and the injection was followed by a negative result.

Watson Cheyne has shown that the *number of bacteria injected makes a very great difference in the result.* He obtained by plate-culture a general idea of the numbers existing in a given quantity of a fluid, the fluid being diluted for the purpose: a certain amount of this material was injected into an animal, and at the same time plates were made from a similar quantity. He thus ascertained quite accurately how many organisms were present in the fluid injected. In the case of the proteus vulgaris he found that $\frac{1}{10}$ cc. of an undiluted cultivation, an amount containing 250,000,000 bacteria, injected into the muscular tissue of a rabbit, proved to be a rapidly fatal dose: $\frac{1}{40}$ cc., containing 56,000,000 bacteria, caused an extensive abscess, from which the animal died in six to eight weeks. Doses of less than 18,000,000 bacteria seldom caused any result. In the case of the staphylococcus pyogenes aureus he showed that it was necessary to inject something like 1,000,000,000 cocci into the muscles of a rabbit to cause a rapidly fatal result, while 250,000,000 produced a small circumscribed abscess. The albus in smaller doses was found to produce the same result. He proved further that the concentration of the bacterial material was of great importance, as shown by the fact that the dose must act at the same place and at the same time. Splitting up the dose and injecting various portions of it into different parts of the animal at successive periods of time or at the same time did not produce the same result. He found also that the dose for different animals varied according to the susceptibility of the animal.

As a human being is not very susceptible to pyogenic organisms, the results produced by them in man vary according to the amount introduced. Consequently, a few cocci entering a wound would possibly do no harm unless, indeed, they met with conditions particularly favorable for their growth, such as the retention of fluid or a clot in which they could readily develop and multiply. This probably accounts for the fairly good results obtained with imperfect aseptic work, the introduction of large doses of bacteria being thus avoided. The pyogenic cocci in small numbers are more liable to cause suppuration if accompanied by a sufficient amount of toxic substances which are present in virulent cultures of the cocci, and the extent of the inflammation bears a relation to the quality and quantity of these substances. In infected cases these chemical products may be found in a much more virulent form than those products obtained from cultures, coming as they do from various sources and growing under varying conditions. The presence in the circulating blood of the toxic products of some micro-organisms favors the development of foci of suppuration, as in pyæmia (Welch).

Before, however, further discussing the questions of the conditions favorable for the growth and spread of the pus-cocci in the living tissues let us consider some of the experiments which prove the pyogenic action of these cocci upon man. Quite a number of such experiments have been made, and some of the most instructive were those performed by Garré, who inoculated with a culture of the aureus a fold of the skin at the edge of his finger-nail, and produced the typical suppuration round the margin of the nail commonly called a "run-around." He next rubbed a large quantity of an aureus culture into the uninjured skin of his left forearm. A burning sensation began at the point six hours later; pustules appeared the following day; the inflammation continued to increase around the pustules, and the fourth day a carbuncle had developed: ultimately there formed more than twenty openings discharging pus and portions of dead tissue. From the pus-discharges a pure culture of the aureus was obtained. This experiment shows not only that the cocci were the cause of the suppuration, but also that they can obtain an entrance through the uninjured skin. It is evident that they must have penetrated through the glandular openings and hair-follicles.

How this process is developed is shown in the experiment of

Bockhart, who rubbed a culture of the aureus into his arm after scraping away the epidermis in one or two places. Pustules and isolated furuncles were developed. A piece of the diseased parts was excised and examined under the microscope. The cocci had grown in between the cells of the exposed rete Malpighii, thence into the papillæ, and also into the hair-follicles and ducts of the sebaceous and sudoriparous glands. There was an active diapedesis of leucocytes from the vessels of the papillæ surrounding the colonies of micrococci, and pustules were thus formed. Bockhart concluded that if the pustule connected with a hair-follicle or a gland-duct, a boil would be produced; otherwise, nothing more than a pustule would be produced. Similar results were also obtained by Wigglesworth.

Bumm injected subcutaneously into his own arm and into the arms of several other individuals a few drops of a salt solution containing fragments of an aureus culture : abscesses varying in size from an egg to that of a fist were thus produced. In one case, when the abscess had not yet fully ripened, he excised the inflamed nodule, together with the surrounding skin and subcutaneous tissue. On section the specimen showed a yellowish, softened centre surrounded by a reddish zone, which gradually was replaced by normal tissue. Under the microscope the centre was seen filled with pus-cells on the point of breaking down into pus, and between the pus-cells were clusters of cocci. On the periphery of the suppurating portion the cocci were seen in large clusters and in columns growing between the wavy fibres of connective tissue, followed by an enormous infiltration of leucocytes. Schimmelbusch, who rubbed a culture of the aureus into the skin of moribund patients and examined the pustules and abscesses thus formed, found that the infection took place through the hair-follicles between the hair and its sheath.

The relative frequency with which the different varieties are found in cases of suppuration in man is shown by an analysis by Steinhaus of 330 cases of different observers. The staphylococci were found in 66.5 per cent. and the streptococci were found in 20.4 per cent. of the cases, and a mixture of the two forms in 9.5 per cent. The tenuis was found only in 1 per cent., and the other forms also quite rarely.

The question now naturally arises : *Is all suppuration in the human subject due to the presence of bacteria?* When Lister first showed that the suppuration of wounds was due to their presence by the very convincing argument of antiseptic surgery, the belief became almost universal that bacteria of some sort are always found as the active agents of suppurations. Previous to that time it had been supposed that mechanical as well as chemical irritation, and also foreign bodies imbedded in the tissues, could produce suppuration. But when the germ-theory had taken a firm hold a school was soon developed, at the head of which was Heuter, whose motto was: "No pus without bacteria." There were many, however, who were not prepared to allow such complete sway to micro-organisms. Billroth held the view that bacteria were not the cause, but were the accompaniment, of suppuration, and that a chemical substance, the "phlogistic zymoid" (a sort of chemical ferment), was the principal agent. Apparently in confirmation of this view there appeared in 1878 a report from Pasteur that he had been able to obtain suppuration with pus in which all the bacteria had been destroyed by heat of from 100° to 110° C.: in other words, from a fluid which contained only the chemical products of those organisms. As the knowledge of the pyogenic cocci became more accurate the disposition was strengthened to regard all suppuration as of bacterial origin.

For the purpose of subjecting this theory to the most rigorous test a large number of investigations were made to determine whether it was possible to cause suppuration purely by chemical substances, such as croton oil, mercury, turpentine, etc. The early experiments of this kind were very contradictory, the errors of many observers being due partly to imperfect asepsis, and partly to the fact that in certain animals suppuration could be produced by those agents that entirely failed when other kinds of animals were used for the experiment. Since then, however, experience has shown the common sources of error, and some of the work has been so carefully performed that it seems impossible to be skeptical of the results obtained.

Councilman was the first to show that croton oil could produce suppuration without bacterial action when injected into the subcutaneous cellular tissue of rabbits. Petrone succeeded in 1885 in obtaining suppuration in rabbits and in guinea-pigs with injections of sterilized pus, thus confirming the experiments of Pasteur. Grawitz and de Bary found that turpentine caused suppuration in dogs, but not in rabbits nor in guinea-pigs. Ammonia, well diluted, if injected into dogs, is absorbed, but in concentrated solutions it causes the formation of pus which proves absolutely sterile to all culture-tests. Cultures of the micrococcus prodigiosus, sterilized by heat and injected, produced sterile pus in dogs, rabbits, and rats. The addition of a small quantity of an aureus culture to this material produced pus very rich in cocci. These authors concluded, as the result of their investigations, that certain chemical substances in certain strengths and injected into certain animals caused suppuration without bacteria, and also that these chemical substances pave the way for the action of bacteria.

Interesting in this connection is the work of Leber, who succeeded in obtaining from cultures of the aureus a crystalline substance to which he gives the name "phlogosin." He has made a number of experiments upon animals with this substance, and he propounds a new theory of inflammation founded on the capacity which, as shown by botanists, is possessed by certain chemical substances of attracting or of repelling certain kinds of organisms. Leber ascribes to phlogosin a similar *chemotactic* action upon the leucocytes, in virtue of which it draws them toward itself. The leucocytes, he thinks, play a double rôle: they absorb the irritating substances and dissolve or digest the necrosed portions of the inflamed tissues. Christmas showed clearly that the conflicting results produced by different observers were due to the varying type of animal used for experimentations. Turpentine and mercury failed with him to produce suppuration in rabbits, but caused suppuration in dogs. He explained this by the slower absorptive power which exists in the latter animals. He obtained suppuration in dogs with bouillon-culture of the aureus, not only after boiling, but also after filtering, the culture. His definition of suppuration is as follows: "Suppuration should be regarded as the effect of a reaction of the tissues against certain chemical substances, whether they are produced by living organisms or are purely chemical in their nature."

Cheyne in his excellent article on suppuration is inclined to take issue with those who maintain that pus can form without bacterial aid. He says: "If a number of careful observers have failed entirely to produce suppuration by the injection of these irritating chemicals, then those who have obtained a contrary result must either have brought some other factor unwittingly into play, or there must be some other explanation of the result." Cheyne, who has carefully gone over the ground, brings forward as evidence the results obtained by introducing hermetically-sealed sterilized glass tubes, containing a mixture of equal parts of croton and olive oil, into the subcutaneous connective tissue. After the wound had healed aseptically the tubes were broken at different intervals of time and their contents allowed to escape. He did not obtain in any case creamy pus, but "a putty-like mass is formed which has been described by some as pus," but which he would not regard as such. It is a question, he says, whether this putty-like material is not a further change of fibrinous exudations produced by the solvent action of the living tissues, which are endeavoring to remove the dead material, and as a result of a prolonged action of living cells on the extensive dead mass.

A number of cases may be found in the quite extensive literature of this subject where it is distinctly stated that there was obtained a considerable quantity of fluid pus containing no bacteria. Steinhaus, who is one of the most accurate investigators of this question, has repeated all the experiments with the greatest care. He found no irritation resulting from the introduction of sealed glass tubes into the subcutaneous tissue: sometimes they became encapsuled, but in the peritoneal cavity they were usually found floating free. He always obtained pus when calomel was used. The "calomel pus" is, however, somewhat different from ordinary pus. The nuclei of the cells are single, cystic, or elongated, and take staining feebly: there appeared to be an advanced degeneration.

Mercury produced suppuration in dogs, rabbits, and guinea-pigs, but the amount of pus produced in the case of the rabbit experiments, the only case in which the pus is described, appears to have been confined to two small clumps of purulent material at each end of the broken glass tube. Nitrate of silver produced "abscesses" in dogs and in cats: of course the pus contained no bacteria. Croton oil produced no pus. It is evident that Steinhaus's experiments with this drug did not differ materially from the experiment of Cheyne. Dead cultures of the aureus injected into dogs, cats, and rabbits produced pus "which was fully identical with the ordinary bacterial pus." Dead cultures of the bacillus pyocyaneus produced pus which had all the gross appearances of ordinary pus. Steinhaus concludes that suppuration can take place without bacteria—that the exciting cause is due to the action of certain chemical substances, which are the products of decomposition produced by micro-organisms and also of inorganic substances like calomel. Other substances than those produced by the pyogenic cocci may also cause suppuration: these are the ptomaïnes of putrefaction, like cadaverin.

From all the above data it must be conceded that *it is possible to produce suppuration without the direct intervention of bacteria, but all are agreed that mechanical irritation or foreign bodies are* *unable to produce suppuration without the aid of bacteria.* A few examples have, indeed, been found of suppuration without pus-cocci. Rosenbach reported hydatids of the liver as the cause in two cases. Baumgarten mentions the jequirity-seed as a cause of suppuration as a clinical occurrence. Possibly the number of suppurative inflammations in which no organisms can be found may with time be increased. Steinhaus suggests that, inasmuch as bacteria are cells or cell-like structures which can produce pus, under certain circumstances the cells which form the animal organism may possibly also produce similar substances. In other words, he says: "Are we not justified in establishing a special class of autochthonous inflammations?" With our present knowledge, a brief sketch of which has been given in the preceding pages, we are not authorized in giving an affirmative answer to this question. It would be misleading to do so.

It should not be assumed that all suppurations are caused only by the three or four micro-organisms already mentioned. It would be fair to say, however, that the great majority of suppurations are caused by these forms. The bacillus pyogenes fœtidus was found by Passet in the pus of a perirectal abscess; it consists of a short staff with rounded ends. The three forms of saprogenic bacilli described by Rosenbach seem to have mild pyogenic qualities, probably in virtue of their ptomaïne-producing power. The bacillus pyocyaneus found in green pus is a short, fine rod, and is very likely to be mistaken for a micrococcus. This bacillus was not supposed to be pyogenic in action, but, according to Steinhaus, its pyogenic qualities have lately been demonstrated. H. C. Ernst has recently also described a fluorescent bacillus taken from the psoas abscess of a child, which bacillus produced abscesses in guinea-pigs on inoculation. Steinhaus has shown that the micrococcus tetragenus is capable of producing suppuration, and he points out that recent experimentation has demonstrated similar qualities in the bacillus anthracis, the typhoid bacillus, and the cocci of saliva described by Biondi. Welch and others have many times found the bacillus coli communis as the cause of suppuration.

The history of the micro-organisms after their introduction into the system must next be followed. This process has been studied by injecting pure cultures of the pyogenic organisms into animals and examining the animals at varying periods after the operation. Ribbert injected cocci taken from an abscess of the bone into the blood, and found that they rapidly disappeared. During the first twenty-four hours they were found in all the organs, and at the end of forty-eight hours in the kidneys only. He concludes, therefore, that the first step in the process of infection is a general dissemination of the bacteria throughout the body, and that subsequently they disappear from most organs, but remain behind in some one organ which contains an embolus or has been damaged. Steinhaus injected 0.5 c.cm. of a pure culture of the staphylococcus into rabbits. No local reaction occurred. The dose was probably not large enough, or the animals were not susceptible to the particular kind of organism used. At the end of six days the animals were killed and cultures were taken from the internal organs, growths of the coccus being thus obtained. It appeared that the organisms disappeared first from the point of injection, next from the liver, then from the kidneys, and finally from the spleen at the end of twelve days. No infection took place, the cocci being carried from the point where they were introduced into the system to the various organs, and were then destroyed, many of them being destroyed also at the point of entrance.

These experiments correspond with Ogston's observation that the cocci are present in the blood in septicæmia without producing suppuration, and that they are excreted in a living state in the urine. Where large numbers are found in the urine Ogston has been able to detect the presence of an abscess by the examination of the urine alone. In Billroth's clinique cocci were found by v. Eiselberg in the blood of individuals affected with septicæmia and traumatic fever, but no cocci were found in the blood of healthy individuals. In septic cases micrococci have been found by Stone and by the writer in the circulating blood.

The rapidity with which the bacteria are eliminated from the system when they fail to get the upper hand is remarkable. According to Cheyne, it is in many cases a matter of minutes merely, certainly of an hour or two. Their disappearance, he thinks, must be due to an active destructive action upon them of the constituents of the blood. Many of the bacteria are probably rapidly eliminated by the kidneys; at least their presence has frequently been demonstrated in the urine, and masses of cocci have been found in the kidneys of children who have died with symptoms of acute febrile disorders.

Experiments on animals with young have shown shortly after the injection the presence of bacteria in the milk, and it is suggested by Cheyne that even the salivary glands and the parotids may be called into action. It is probable also that many bacteria are removed through the intestinal mucous membrane, and some have even been traced into the respiratory organs, and have finally found their way out of the body in the expectoration. The old idea of "appealing to the emunctories" thus receives a scientific endorsement.

When the conditions for suppuration are favorable an *injection of staphylococci* into the subcutaneous tissue of an animal will cause an abscess. Baumgarten thus describes the result of such an injection: The staphylococci multiply rapidly; they grow into the fibrillated intercellular substance and also into the pre-existing cells of the tissue and the vessel-walls; already twenty-four hours after the injection exudation and diapedesis begin; enormous numbers of polynucleated leucocytes are found between the fibres of the tissue; the fibres are more or less swollen, and the lymph-spaces are distended and partly filled with large, round, finely-granulated cells, which are the altered fixed connective-tissue cells, and partly with clumps of leucocytes, near which are seen the large cystic nucleus of the neighboring fixed cell; the small vessels are dilated and distended with blood, and in many places lined with leucocytes; the coccus-growth becomes more and more vigorous and tends to group into masses; a number of cocci are found in the leucocytes and fixed cells, the thickest growth, indeed, being intracellular; no difference in form or coloring is observed between those organisms lying in and those lying between the cells; in the centre of the inflamed focus the coccus-growth and the infiltration of leucocytes form a more or less continuous mass, except that the cocci still show a tendency to aggregation in groups; on the second or third day the tissues at this point begin to soften and liquefy, and the result is an abscess; at the periphery of the inflamed mass the coccus and leucocyte infiltration continues to spread; the cocci grow in thick columns, with small groups here and there along their borders, which groups separate and grow into the surrounding tissue.

Bonome, who experimented with the aureus in order to produce a lung-abscess to show that the cause of the suppurating abscess was not the pneumonia coccus, describes a central necrotic zone which included more or less the débris of the leucocytes that had immigrated; outside this necrotic zone was a granular zone of leucocytes; outside this granular zone was a hemorrhagic zone; and surrounding all was a zone of catarrhal pneumonia. This formation he terms a furuncle of the lung, and, anatomically considered, is a counterpart of what occurs in furuncle of the skin.

This result is at variance with what Baumgarten observed in his subcutaneous injections of staphylococci. Baumgarten attributes the occurrence of necrosis of the tissue involved to the number of cocci used for the experiment, and he shows that when other observers employed much less concentrated doses of these organisms no such necrosis of the lung took place. Watson Cheyne in his lectures on suppuration accepts this view of a coagulation-necrosis of the tissues in abscess-formation, and it is therefore important to state just what view Baumgarten takes on this point. Baumgarten concludes that the occurrence or the non-occurrence of such a necrosis depends upon the number of cocci originally introduced and on the rapidity of their growth. There may occur such a necrosis as Bonome describes in the lung and also in furuncle, but it would not probably take place in the subcutaneous connective tissue. Necrosis is more likely to occur in tissues not richly supplied with blood-vessels, such as the valves of the heart, the deleterious action of the cocci being expended upon the tissue before diapedesis takes place and the leucocytes make their way into the infected district.

There is a marked difference in the *action of the streptococcus.* It does not possess the same tendency to promote local suppuration that is seen in the case of the staphylococcus. It possesses a peculiar faculty to creep along through the tissues without producing suppuration. The short life of the staphylococcus and its tendency to break down the tissues do not favor its spreading. According to Ogston, after the injection into animals the chains of cocci insinuate themselves between the cells and the fibres of the tissue and form a sort of network, and a "waxy" change occurs in the parts thus involved. Eventually there forms a protecting wall of granulation tissue which prevents further progress; but before this wall forms septicæmic symptoms prevail, and micrococci in pairs and in chains are found in the blood: as the granulation tissue develops the constitutional symptoms subside and the organisms disappear. According to Baumgarten, the streptococcus is not so well adapted to growth in the body of an animal as the staphylococcus. When, however, it does grow, it produces a spreading inflammation, more like erysipelas, or a superficial form of suppuration with less tendency to a breaking down of the tissue involved. It is well to remember here that the behavior of these two forms of cocci in the living tissues corresponds with what has been noticed in the gelatin-cultures. The staphylococcus exerts a strong peptonizing action upon the culture-soil, and liquefaction takes place. Its tendency to form pus in the tissues is equally well marked. The streptococcus, which does not have the same tendency to produce suppuration, fails to peptonize and liquefy the gelatin. It has been observed, however, that when deprived of oxygen the streptococcus does exert a decided peptonizing action on boiled albumin and beef; consequently under favoring conditions it might be expected to cause suppuration, and this action it does exert during the later stages of the period of its invasion of the tissues.

As has been seen, it is necessary that a certain number of the pyogenic cocci should gain entrance into the system, otherwise they soon disappear; but if a sufficient number has taken foothold they will be carried into the general circulation, either through the lymphatic system by the process known clinically as *lymphangitis*, or direct into the venous circulation by gaining an entrance to a large vein near the inflamed part. The cocci invade the vessel, and there set up an inflammation which terminates in a breaking down of the endothelium and the formation of a thrombus. (See *Pyæmia*, p. 361.) This thrombo-phlebitis terminates in a breaking down of the thrombus, and emboli form, which spread the organisms in various directions. When circulating free in the blood they soon disappear from the general current, being found in the endothelium of the capillaries in organs where the stream is slow (as in the marrow of bone), in the glomeruli of the kidney, and in the spleen and liver.

In whatever way they may have been carried to the part, the bacteria, when once established there in sufficiently large numbers, bring about the formation of an abscess; for instance, a clump of cocci, when once caught in the capillary of a kidney, fill out the vessel. In the centre of the mass the organisms are hard to distinguish, but at its border the individual organisms are distinct. The obstruction gives rise to an accumulation of leucocytes, which may also be seen within the vessel. The cocci next work their way through the capillary wall into the surrounding uriniferous tubes, and here is soon seen a change in the character of the kidney epithelium, the nuclei losing the staining power and being seen only with difficulty. These are the first changes which indicate the formation of a coagulation-necrosis of the tissues of the part. Leucocytes now emigrate from the neighboring vessels. If the district involved is of any size, a portion of the kidney is eventually destroyed, and in the centre of the necrosed portion is found a mass of micrococci. This is the type of *abscess-formation* so well described by Cheyne. He says: "Staining sections of tissue in which these plugs are present with ordinary aniline dyes, it is found that, while the mass of organisms is internally stained and while the nuclei in the section have become well colored, there is a ring of tissue around the central mass of organisms which does not take on the stain, and which presents a homogeneous, translucent appearance. This ring evidently results from the action of the concentrated products of the micrococci, the tissue being brought into the condition of coagulation-necrosis. After some hours a second ring appears at a greater distance from the mass of organisms, this ring being composed of a dense layer of leucocytes apparently collecting where the chemical substances are more dilute and do not interfere with the life of the cells. As time goes on the intermediate translucent layer becomes infiltrated, on the one hand with cocci from the central plug, and on the other hand with cells from the outer ring, and the original tissue rapidly disappears, probably as the result of the peptonizing action of the cocci. At the same time the fluid effused does not coagulate, probably also on account of the peptonizing action of the cocci on the fibrinogen, and thus we come to have a central collection of fluids containing leucocytes and micrococci, surrounded by a wall of leucocytes and cocci—in other words, an abscess."

The quality which the streptococcus possesses of producing a coagulation-necrosis is shown in its tendency, when it invades a mucous membrane, to produce a diphtheritic inflammation. This tendency is seen in the initial stages of puerperal fever when the vaginal and uterine mucous membranes are first invaded by the streptococci. The feeble peptonizing power which the streptococcus possesses at first appears to gain in strength after remaining some time in the tissue, and, accordingly, in the later stages of puerperal fever the same organisms seem capable also of developing metastatic suppuration. In erysipelatous inflammations the streptococcus does not remain long enough in the skin to acquire this property; consequently it is found that abscess-formation in this disease is rare. Its growth in the subcutaneous tissues produces at first a fibrinous or a sero-fibrinous inflammation; consequently, local circumscribed collections of pus or abscess-formations do not take place in many cases.

As already stated, considerable numbers of organisms may be injected into the body of an animal and may disappear with great rapidity. *Under what circumstances do we find an active growth of these organisms?* Cheyne, who has treated this subject at some length, first calls attention to a point about which more will be said in discussing the etiology of pyæmia. Suffice it to say here that certain *mechanical conditions* are often necessary to enable the cocci to obtain a lodgment in the tissues. Thus, Ribbert was unable to obtain multiple abscesses in rabbits by injecting moderate quantities of cocci into the circulation, but if the organisms were mixed with fragments of the potato on which they were grown, he was then able to obtain deposits of the organisms in the muscular tissues of the heart as well as in other organs.

But it is not simply necessary that the organisms should obtain a lodgment: *the state of the tissues* in which they are arrested is an important factor also in the question of suppuration. Experiments on animals seem to show that a diminution in the vitality of the part is favorable to their development. Thus, Cornil was able to obtain septic nephritis by ligaturing the renal arteries for some time, and, after removing the ligature, by injecting pyogenic cocci into the circulation.

Analogous to this are the well-known experiments of Kocher, who produced osteomyelitis in animals by injecting certain chemical substances into the medulla of their bones and afterward feeding them with putrid food. Septic infection, taking place through the intestinal canal, found its way to the injured part. The same result was obtained by fracturing bones and injecting cocci into the circulation.

Cheyne has studied the influence of inflammation in favoring the growth of bacteria in a part. In the first stage of inflammation the vital activity of the tissue is suspended; the second stage is that of healthy vigorous granulation; and in the third stage the cicatricial tissue is a less active type of growth.

Huber set up an inflammation in a rabbit's ear with croton oil, the other ear being left intact for purposes of comparison: anthrax bacilli were then injected into the tip of the tail. During the first stage of inflammation there was a very marked increase in the number of bacilli in the capillaries of the inflamed part as compared with the number present in a similar part of the opposite ear. As the inflammation passed into the second stage the number of bacilli in the capillaries of the inflamed part gradually diminished, until, when this stage was at its height, the bacilli had completely disappeared, although they were present in large numbers in the capillaries of the other ear. During the third stage, when the inflammation had subsided, the bacilli again appeared, and were found in considerable numbers in the newly-formed vessels.

Cheyne argues from these experiments that severe inflammation does not tend to a deposit in the part, but that in less severe inflammation the pyogenic organisms may pass out of the vessels and set up suppuration. Thus acute osteomyelitis and local tubercular diseases frequently stand in some relation to injury. They are not, as a rule, attributed to severe injuries, but to some slight blow or a sprain. As Cheyne points out, injury is an important predisposing cause for suppuration; it may act in two ways: not only in the manner above referred to, but also by leading to an effusion of blood, thus enabling the pyogenic cocci which may be circulating in the blood to pass out of the vessels and find in the cellular tissue a suitable place for their development. The laceration of the valves as an element in the artificial endocarditis alluded to farther on, and the experimental fracture of bones above mentioned, are examples of the effects of injury in promoting infection. Anything interfering with the integrity of the tissues is a predisposing cause of suppuration. Irritation with strong antiseptics may, as Halstead has shown, lower the vitality of the surface of a wound and thus favor suppuration. Bruising and tension of the tissues are also predisposing causes. Dead spaces and foreign bodies remove bacteria from the influence of the living tissue and the fluids, and thus place them in conditions more favorable for their growth.

The anatomical arrangement of the part may also prove a very important factor in the production of suppuration. In acute osteomyelitis the inflammation is limited to certain bones and to certain parts of bones, such as the epiphyseal line in long bones. This predilection may be explained by the presence of a large area of growing young tissue, by the vascularity of the part, or by the slowness of the circulation.

The state of the blood is also of importance, as exhibited by the well-known tendency of carbuncle to form in cases of diabetes. Whether the presence of sugar in the blood directly favors the action of the pyogenic cocci does not appear to have been proved satisfactorily, and experiments upon this subject are conflicting. It is probable that the diminished vitality of the system is a more probable cause than the presence of sugar. Gärtner's experiments show that, with small quantities of the aureus, infection more readily takes place in anæmic subjects, thus explaining the frequency of boils in individuals who are not in a robust condition of health.

The literature on the question of the *season of the year* as an influence affecting suppurative disease presents nothing of special scientific value. In the winter months, when hospital wards are imperfectly ventilated, the number of cocci in the air is increased. In the close and squalid dwellings of the poor in large cities the conditions are much more favorable for the growth of pyogenic organisms than they are in country dwellings in a good sanitary neighborhood.

According to Cheyne, acute osteomyelitis is reported exceedingly prevalent in certain parts of Switzerland and Germany, but the writer doubts whether *locality* has any special influence upon the disease. Notwithstanding the greater prevalence in Europe of bone-deformities from rickets and other diseases, which is apparent even to the layman's eye, the writer is inclined to think that suppurative diseases of bone occur quite as frequently in America.

The conclusions which may be drawn from all these studies of the etiology of suppuration are—that *in man, with few rare exceptions, suppuration is caused by micro-organisms, and that in the great majority of cases these organisms are staphylococci or streptococci.* Experimentally, suppuration can be obtained by purely chemical substances, such as calomel, or by the ptomaïnes derived from the action of organisms upon living or upon dead substances. The practical conclusion to be derived from such experiments is that *chemical substances play a prominent part in the production and the spread of suppuration, but they are dependent upon organisms for their development.* These substances are liberated by the cocci either from themselves or from the tissues from which they derive their nourishment. The pyogenic cocci cannot, however, always produce suppuration; the living healthy tissues are antagonistic to them. They gain an entrance and are able to grow only when present in sufficiently large numbers. Even then they may be dissipated if the absorptive power is sufficiently active. But if the vitality of a part is lowered by traumatic inflammation, or if there are large effusions which cannot readily be absorbed, then they find a soil favorable for their growth. The pus-producing power of the pyogenic cocci seems to lie in their ability to liquefy the fibrinous exudation of inflammation. In large numbers or in certain forms they exert a chemical action upon the tissues which produces a necrosis. Their elimination from the body may occur either through death of the bacteria in various organs or by the action of excretory organs. To what extent they are excreted is not yet clear. It is probable that the leucocytes are engaged in a struggle with the cocci, and that pus exerts a deleterious action upon the organisms through the chemical substances evolved. It is probable also that bacteria die rapidly in pus from phagocytosis or from starvation, and pus is a vehicle in which they are discharged from the body. Fatal infections from the cadaver are not usually marked by local reactions or by suppuration. The process of suppuration may therefore be regarded as serving a useful purpose, and is one of the most important weapons employed by nature in resisting the invasion of bacteria.

This branch of the subject cannot be passed by without some allusion to the question of *immunity*.

Bacteria may bring about diseased conditions by the action of an albuminoid substance which they possess in their bodies, and which is thought by some to be liberated during the process of degeneration of the microbe. This substance is known as a *bacterial proteid*. They may also produce disease by the formation of a toxic substance in the tissues during their growth.

In the former case an intoxication is produced by the absorption of a poison developed by the bacteria themselves. In the latter case the tissues are so modified by the proteids that there is formed in them a chemical substance known as a *toxalbumin*, which, being absorbed, produces the constitutional symptoms, and in suppuration causes the destruction and degeneration of the attracted leucocytes, which thus collect as pus.

Immunity is quite a complex condition, and it appears to exist in certain individuals in virtue of a chemical substance, found there or formed as the result of bacterial action, which is either hostile to their development or acts as an antidote to the poison they produce. It is also brought about by the action of the bacteria in producing an inflammatory reaction in the tissues, as the result of which a large number of phagocytes make their appearance in the tissues.

This power of attracting cells is known as *chemotaxis*, and is due to chemical attraction or to irritation produced by the proteids of the bacteria. The chemotactic action of pure protein, as it is found in cultures of bacteria, is very intense. This attraction can be exerted by bacteria whether living or dead; it is not confined, however, to bacteria. Products of other living substances can act as chemotactically as those of bacteria.

The proteid material may also be liberated by disintegrating tissues, and the process of absorption may in this way be brought about, the leucocytes thus attracted carrying away a certain amount of refuse in their bodies. This power is possessed by finely-powdered substances in different degrees. Gold, silver, and iron exert very little irritation of this kind, but copper and mercury are highly chemotactic. Chemotaxis is said to be positive or negative according as there is attraction or repulsion.

Metschnikoff thus explains how immunity is effected from a certain disease after one attack. Chemotaxis, being variable, may be converted from positive to negative, or vice versâ. In mild forms of infection substances may attract cells which in virulent forms they repel. If a mild or attenuated virus is used, chemotaxis, at first negative, will change to positive, and the phagocyte will thus be induced to attract or attack the invading element of disease. The Metschnikoff school, on the one hand, finds a sufficient explanation for immunity in phagocytosis alone. The German school, on the other hand, points out that the leucocytes may exert a phagocytic action if the bacteria are present, but repair and cure may also take place when the chemical products alone of bacteria are present. In such cases they are agreed that the process is due to an antidote—a protective or defensive proteid or antitoxine—which may be the product of these cells or be furnished from the blood. In fact, the normal tissues seem to possess the power of rendering inert many kinds of organisms which may have gained access to them. The antiseptic properties of blood-serum are now generally recognized. These properties are due to the existence of a substance known as *globulin*. Hankin has isolated from the spleens and livers of various animals a proteid having the power of killing bacteria, and he has found that this substance, though absent from normal blood, may be obtained from the blood of febrile animals—an interesting point throwing light upon the propriety of attempts to reduce fever in septic cases. It was therefore inferred that those animals which were refractory to certain diseases, and those made immune by vaccination, would be able to produce defensive proteids; and this has been found to be the case.

In certain cases the blood-serum is found to destroy the poison produced by the bacteria, but not the bacteria themselves; that is, the serum is antitoxic. Hankin thus defines immunity: "Immunity, whether natural or acquired, is due to the presence of substances which are formed by the metabolism of the animal rather than that of the microbe, and which have the power of destroying the microbes against which immunity is possible or the products on which their pathogenic action depends."

If the nature of these protective substances could be determined and they could be extracted from the blood, the physician would then possess the power of neutralizing disease. Behring and Kitasato have already experimented successfully in this most important and suggestive field of therapeutics. They have not only been able to render animals immune to certain diseases, and to check the course of the disease when it was already well advanced, as in hog cholera, but they have also been able to apply these principles to certain diseases of man, and their success in the treatment of diphtheria and tetanus has raised hopes for a brilliant future in this line of therapeutics.

VII. INFECTIVE INFLAMMATION.

2. SUPPURATION.

SUPPURATION takes place in the tissues by virtue of the peculiar peptonizing or digestive action which the bacteria exert upon them. When this action is exerted in an intense degree the chemical substances produced bring about a change in the cells and in the intercellular substance of the part known as *coagulation-necrosis*, whereby the cells grow more indistinct and do not react in a characteristic way to staining reagents, and the intercellular substance assumes a more or less homogeneous appearance. A necrosis of the tissues is not always necessary to produce suppuration, but the changes in the affected tissues are what one would expect from an intense irritation. In the beginning the same changes that occur in the lighter forms of inflammation are noticed. Some œdema of the part is first observed, with an increase in the size of the fixed cells and a proliferation of these cells, and karyokinetic changes may be found in many of their nuclei. At the same time there is a large accumulation of leucocytes, and the intercellular substance undergoes a mucous softening which gives it a homogeneous or a granular appearance. The mucous transformation of the intercellular substance is the beginning of the softening of the tissues, and at this time there may be found, in sections of such tissue, red blood-corpuscles mingled with cells in mitosis and young tissue-cells. As the zone of pus is approached the leucocytes preponderate over all other types of cells, and the intercellular substance becomes still softer. At this point also are seen pyogenic organisms in considerable numbers: as the virus acts more and more intensely on the part the cell-structures break down, being digested, as it were, by the chemical substances, and the intercellular substance liquefies, and there results a fluid—namely, pus—in place of a solid material.

There are two forms of leucocytes—the single-nucleated and the polynucleated. The polynucleated cell, which is the type of the pus-corpuscle, possesses two or three nuclei, or peculiarly deformed, biscuit- or sickle-shaped nuclei. The nuclear changes are not supposed to be those which precede cell-division, but are more probably indicative of a breaking down of the nucleus.

The single-nucleated cell is not seen in large numbers in acute inflammation, but in later stages of the latter and in chronic forms it is more common. The nucleus is larger than that of the pus-cell. It comes from the blood, but the tissue-cells produce also similar cells called "wandering cells" (Ziegler).

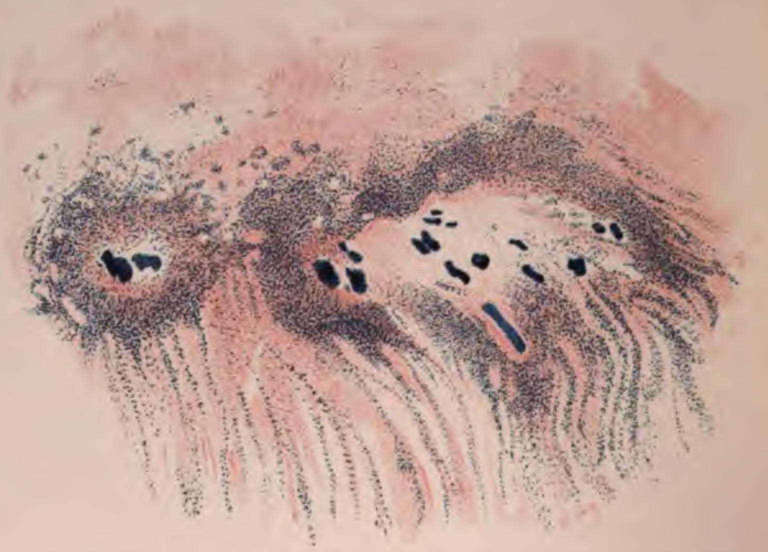

FIG. 27.—Metastatic Abscess of Kidney: plugs of micrococci in central necrosis, with surrounding cell-infiltration (oc. 3, obj. A.).

If the bacteria have accumulated in a mass at any given point —as, for instance, in a capillary loop of the kidney or in the soft succulent tissue of a bone—the concentration of the virus produces a coagulation-necrosis of the immediately surrounding tissue, and there is developed a central point around which the abscess forms. The leucocytes soon accumulate in enormous numbers around such a mass of dead tissue, and if the abscess is examined at this stage there will be found in the centre of it a cluster of micrococci imbedded in a mass of necrosed tissue, forming a more or less transparent zone around them (Fig. 27). Surrounding this mass of broken-down tissue is a wall of leucocytes. As the abscess grows in size the leucocytes wander into the necrosed area and mingle with the micrococci. Many of the foremost ranks of the walls of leucocytes are separated from their neighbors by the liquefaction of the intercellular substance, which liquefaction is caused by the peptonizing action of the bacteria. In this way the area of fluid material is constantly enlarged. In the outer portion of the wall of leucocytes many fixed cells of the surrounding tissue are to be found in a state of proliferation. The growth of the abscess-cavity is caused by the bacteria invading the surrounding tissues and the progressive softening which takes place in the way indicated. The tension of the tissues over some point in the abscess-cavity becomes very great from the pressure of the enclosed fluid, and the vitality of the tissue is also impaired by the septic infection; softening or necrosis takes place, and the abscess "points" and breaks and the contents are discharged. An abscess may therefore be defined as a circumscribed collection of pus.

The tissue lining the walls of the abscess-cavity is called "granulation tissue," and it is by the growth of this tissue that the cavity is filled up and repair is effected. The tissue thus formed consists chiefly of small round cells with very little intercellular substance, and is very rich in capillary blood-vessels. The polynucleated cells, which are numerous, are cells which are breaking

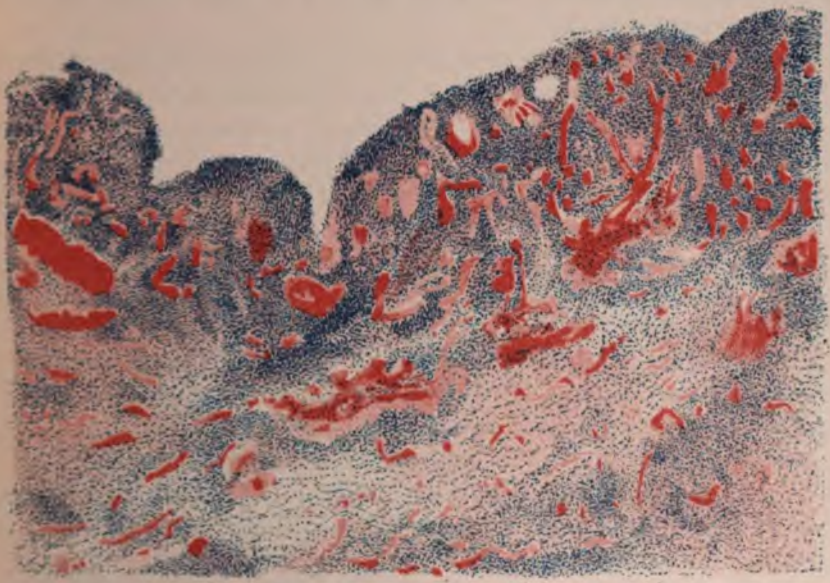

FIG. 28.—Portion of Wall of Lung-abscess, natural injection (oc. 3, obj. A.).

down and about to be thrown off from the surface as pus-corpuscles or to be absorbed or to serve as food for the cells which are building up new tissue. There are also a number of leucocytes with single nuclei, and of larger cells each with a large oval bright nucleus, which are called "epithelioid cells" from their resemblance to epithelium. These cells are also called "fibroblasts," which presently become more numerous than the pus-cells, and which are the active agents in the process of repair, as will presently be seen.

The wall of the cavity is at first lined with pus and shreds of broken-down tissue, but when all this has been discharged the lining membrane is found to consist of a richly vascular tissue studded with numerous little red nodules, which are called "granulations," and the tissue of which they are composed is the granulation tissue above described (Fig. 28).

The group of symptoms which characterize suppuration gives a picture of septic inflammation of the most marked type. The formation of an abscess is accompanied by a great amount of swelling of the surrounding tissues, which are made tense and brawny by the exudation with which they are infiltrated. A bright red blush extends even to the surrounding tissues. As the tension increases the pain becomes acute and is of a throbbing or of a boring character. The constitutional disturbance is also great, and the advent of suppuration is usually indicated either by a chill or by a sudden rise of temperature.

As the pus approaches the surface the tissues near the centre of the inflamed area become softer, and on pressure with the fingers are said to "fluctuate." The integuments, however, are tense, and they become stretched and thinner, and finally a whitish spot indicates the near approach to the surface of the fluid contents of the abscess. At this stage the pain is most acute and the febrile disturbance is usually at its highest point. When the abscess breaks and the pus discharges freely, both local and constitutional symptoms subside.

The surface of the abscess-wall is now found covered with shreds of broken-down tissue. On scraping this tissue away a layer of firmer tissue, the granulation tissue is reached which separates the suppurating area from the surrounding tissues. In two or three days the wound "cleans off," and the shreds are discharged with a flow of pus, and red granulations are seen lining the walls of the cavity.

Pus is a yellowish-white substance of the consistency of cream, and, in what may be said to be its natural condition, is odorless and has an alkaline or faintly acid reaction; under the microscope pus is found to contain a large number of cells known as *pus-corpuscles*. When this fluid is allowed to stand for several hours a sediment is formed which is composed almost entirely of these corpuscles. There are also found some broken-down tissue-cells, fragments of fibrous tissue, and various forms of bacteria, principally the pyogenic cocci (Fig. 29). There is a certain amount of granular débris,

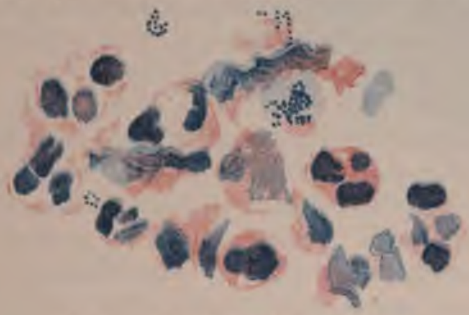

FIG. 29.—Pus-cells with Staphylococci.

which is the result of the breaking down of leucocytes and blood-plaques. The *liquor puris*, or pus-serum, is a pale, yellowish fluid, which differs somewhat from blood-serum in containing the products of the decomposition of tissues during the suppurative process, such as leucin and tyrosin. Pus-serum also contains a substance known as *peptone*. The principal source of the pus-cells is the

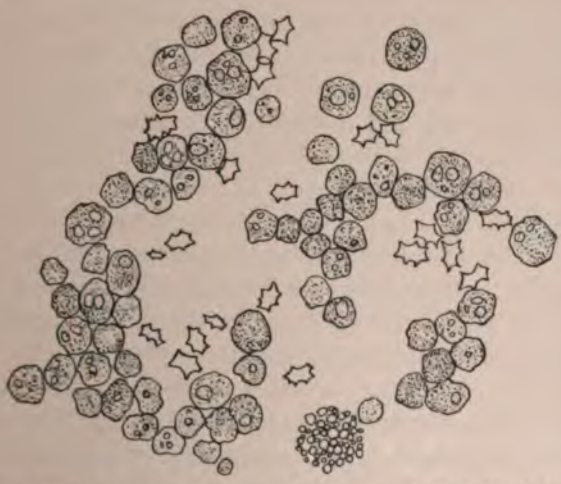

FIG. 30.—Pus-cells treated with Acetic Acid, and Crenated Red Blood-corpuscles (oc. 4, obj. D.).

blood, from which the leucocytes migrate to the focus of suppuration. When treated with acetic acid and the various staining methods these corpuscles (Fig. 30) are found to contain several nuclei. This polynuclear condition is not a sign of cell-activity, but rather one of degeneration. Many of the cells, however, when examined in the fresh state, have amœboid movements. The tissue-cells are represented to a certain extent among the pus-corpuscles, but their number is quite limited. The polynuclear leucocyte should therefore be regarded as the type of the pus-corpuscle. Micrococci are rarely seen in the interior of pus-cells, but they are usually found between them floating in the pus-serum. Pus was formerly known as *good* or *laudable pus*. Until recently several varieties of pus have been described, but the names given to them are now but little used.

Ichor is a name given to pus in a state of decomposition. The pus-cells are few in number and the bacteria of decomposition abound.

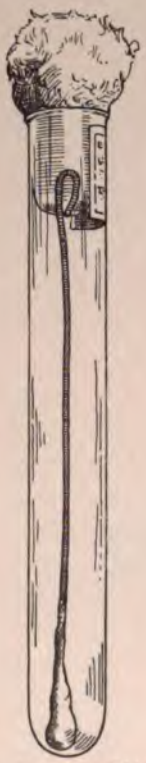

FIG. 31.—Sterilized Test-tube and Swab for collecting pus and fluids for bacteriological examination.

Sanies is pus usually in a more or less decomposed condition, and is mixed with blood. These forms of pus are very irritating and have either a strongly acid or an ammoniacal reaction.

Blue pus is caused by the presence of the bacillus pyocyaneus. It has no special significance and is rarely seen. In acute forms of septic inflammation deposits of an *orange color* are occasionally found on suppurating surfaces. This color is due to the presence of hæmatoidin crystals, the result of the presence of red corpuscles in the exudation. It is thought by Verneuil to indicate an unfavorable prognosis.

Tubercular pus, which is a pale, chalky fluid, contains but few pus-corpuscles and no pyogenic cocci. The sediment consists of the products of broken-down tissue and of a few tubercle bacilli.

Red pus has recently been described by Ferchmin. It is said to be due to the presence of a bacillus whose length is about one-third the diameter of a red blood-corpuscle. The bacillus has no spontaneous movements and is colorless, but it is readily stained by Gram's method. It grows best at a temperature of 36° C. The cultures on blood-serum have a bright red color, which later changes to violet. It was observed in fourteen cases in the clinic at Charkow. The red pus is best seen on the white dressings when first removed. It can readily be distinguished from blood with little practice. If allowed to dry upon the dressing, it does not change color, whereas blood spots soon become a dirty-brown color.

3. ABSCESS.

Abscesses may in a general way be classified (1) as superficial or subcutaneous, and (2) as deep-seated or subfascial. *The pus as it forms spreads in the direction of least resistance*, and an abscess may thus become very greatly enlarged. The loose subcutaneous tissue offers a favorable route for the extension of the inflammatory process, while the fascia presents great resistance, so that the superficial abscess may spread horizontally for a considerable distance, instead of burrowing down into the tissues beneath.

The *subfascial abscess* dissects its way along the sheaths of the muscles and blood-vessels, and may even separate the periosteum from the bone. The anatomical arrangement of the fasciæ and the space which they enclose often determines the route these abscesses pursue.

In the neck, for instance, will be found the deep cervical abscess, which forms in the upper triangle of the neck in one of the lymphatic glands situated near the angle of the jaw, and burrows downward, sometimes to the anterior mediastinum, owing to its inability to penetrate the deep layer of the cervical fascia. A still deeper abscess in this region is the retropharyngeal, or the "retrovisceral abscess," as it is sometimes called. This abscess occupies the space between the œsophagus and spine, which space is filled with loose connective tissue, permitting the pus to burrow downward into the posterior mediastinum. Laterally, this space is shut in by the sheath of the blood-vessels, which is quite unyielding in the upper portion of the neck, but at the level of the inferior thyroid artery the connective tissue becomes loose again, and permits pus to escape from the retrovisceral space into the previsceral region, where it may burrow upward in front of the carotid sheath. These spaces may artificially be injected in the cadaver through a canula introduced beneath the mucous membrane of the pharynx, through which fluid can be forced from the posterior space along the sheath of the inferior thyroid artery to the anterior spaces of the neck. Pus in this region may find its way to the surface near the angle of the jaw, but more frequently it burrows downward in the way indicated. Such an abscess usually originates from a tubercular nodule in the body of a vertebra. The subfascial abscess may also take its origin from an inflammation arising from an adjacent organ, as the kidney, giving rise in this case to the so-called "perinephritic abscess."

The earliest symptoms of such deep abscesses are of a subjective nature. A slight œdema may be seen locally at first, but no swelling nor redness. In a few days there is evidence of deep-seated infiltration and the part becomes tender on pressure. As the inflammation approaches the surface all the symptoms become more marked. Several days may elapse, however, before the pus reaches the surface. At this time the skin is tense and of a scarlet redness, the contour of the adjacent parts is lost, and there are dense infiltration and œdema of the surrounding tissues. When the pus is discharged foreign substances may be found mixed with it, such as fæces, urine, or fragments of bone, according to the source from which it comes.

Phlegmonous inflammation is a term given to the spreading forms of suppuration, such as are usually produced by the invasion of the streptococci. Here all the signs of acute inflammation are present and the area involved is extensive. The connective tissue and the lymphatics are the routes through which the streptococci spread. These organisms do not cause suppuration at first, but as they grow they exert a poisonous influence upon the tissues wide-spread in its effects. If an incision is made into the part during the early stage of the process, there is set free a more or less clear, yellowish fluid, which may contain a few pus-cells or flakes of fibrin. Nearer the central point of the inflammatory process the cut surface has a pork-like aspect. As the streptococci dévelop in the tissues more extensively, a coagulation-necrosis results from the intensity of the virus, and finally foci of suppuration are established. A considerable portion of the tissue may become necrosed, with the formation of sloughs, and the skin may become separated from the parts beneath. In many portions of the inflamed part the veins are found to be filled with thrombi, and when such tissues are incised the amount of bleeding is often strikingly small.

This form of inflammation is usually accompanied by an œdematous swelling of the parts. In the more central portion the tissues become hardened and brawny, and the natural folds of the region are more or less completely effaced. On the surface of the distended skin appear vesicles filled with red or yellow serum.

The constitutional disturbance is usually profound and of a septicæmic character. When suppuration is established, pus may come to the surface at one or more points. If the pus be evacuated and the finger be introduced through the opening made, a series of spaces are felt between the skin and the muscles, or the pus may be found to have burrowed between the muscles and vessels down to the periosteum. The type of such an inflammation may be found in those septic processes which develop in the hand and spread rapidly up the arm. Here is found not only a continuous spreading inflammation of the connective tissue, but also an involvement of the lymphatics, as shown by red lines running along the inner aspect of the arm to the group of glands at the elbow or the axilla. Occasionally the suppurative process will develop itself at one of these two points, a protective influence being thus exerted by the lymphatic glands, by which a further spread of the process is prevented. A good example of phlegmonous inflammation is seen also in a case of compound fracture which has become septic. In fractures of the leg of this type the soft parts extending from the ankle to the knee may thus become involved. The most severe form of this inflammation is seen in phlegmonous erysipelas.

In rare instances a more grave type of inflammation is developed, known as *malignant œdema.* In this type the rapidity and intensity of the process are such that the tissues seem to become extensively necrosed, or the patient succumbs to acute septicæmia before suppuration is established. The streptococcus frequently plays a prominent part in this inflammation, though occasionally there is found the organism known as the *bacillus of malignant œdema.* A whole extremity may become involved within from twenty-four to thirty-six hours in a diffused œdematous swelling. The skin is not reddened, but has a brownish color, and becomes still more discolored, and later assumes a more or less cadaveric appearance. In the early stages an incision evacuates only a serous fluid which here and there has a slightly turbid appearance, suggestive of the presence of pus-corpuscles. Later, free and deep incisions show that the process has involved all the soft parts of the limb, and that the subcutaneous tissues, and even the muscles, may have become gangrenous.

An example of this type of inflammation was seen a few years ago in the case of a medical student. The young man, who had been in somewhat feeble health, had wounded a finger in the dissecting-room. When seen on the second day of the disease the whole arm to the shoulder had become involved, and the process had extended to the adjacent tissues of the thorax. Free incisions were made by his surgeon over the pectoral muscles and into the upper part of the arm, which incisions gave vent to an abundant flow of a slightly turbid serum, no pus being found anywhere. The process could not be arrested, and the patient succumbed to septicæmia on the following day.

An elderly carpenter came into the hospital recently with an injury of his hand from a splinter of wood. The whole upper extremity was involved in a septic process of three days' standing, and the constitutional disturbance was profound. The patient was etherized, and free incisions showed that pus had burrowed into the deepest intermuscular spaces and that the connective tissue was everywhere gangrenous. The operation gave no relief, and the patient died of a typical acute septicæmia on the following day.

The *treatment of a circumscribed abscess* consists in early incision for the evacuation of pus. The old method consisted in the application of poultices until the abscess "pointed," when an incision hastened the escape of pus by a few hours only. In many cases such delay may endanger important structures and allow the abscess to attain a size which will require a long time for the wound to heal. An incision should therefore always be made as soon as the diagnosis of suppuration is established. The only exceptions to be given to this rule are those cases in which the abscess is not liable to spread and involve important structures, and in which the patient prefers to wait for the slower method of Nature.

Antiseptic precaution should not be relaxed in these operations. The parts should be cleaned thoroughly beforehand, and the operating instruments and the hands of the operator should be disinfected. A clean-cut incision should be made of sufficient length to keep open the most prominent or the most dependent part of the abscess throughout its whole length. In very large abscesses it may be preferable to limit the length of the incision and make, if necessary, a counter-opening. Very long incisions are rarely necessary where the suppuration is circumscribed. When the opening has been made the edges of the wound should be separated and the inner surface of the cavity be inspected, all sloughs and infected tissue being removed as carefully as circumstances permit. This removal can best be performed with a sharp curette. The wound should then be irrigated with a solution of corrosive sublimate of a strength of 1 : 1000 or 1 : 5000, and, after drying, it should be stuffed with iodoform gauze and a dry dressing applied; or there may be employed an antiseptic poultice consisting of absorbent cotton soaked in a very weak solution of carbolic acid or creoline or corrosive sublimate (1 : 20,000). An antiseptic poultice should always be used when the incision has not been large enough to lay the cavity thoroughly open, and the cavity should be drained by a rubber tube inserted through the wound. These wet dressings should be changed every two or three hours when the discharge is free. The dry dressing may be allowed to remain for twenty-four hours, or even longer when the infected tissues have been thoroughly removed. When the latter method is successfully employed, all further infection is checked, the inflammation subsides, and the wound becomes in two or three days a healthy granulating surface.

Every abscess should be thoroughly disinfected when it is possible to do so. Prompt and energetic treatment of this kind is especially indicated in abscesses involving a portion of the peritoneal cavity to ward off a general peritonitis, or in the neighborhood of the rectum to avoid the occurrence of a *fistula in ano.* Deep-seated abscesses of the neck come within this category, as they are liable to burrow freely among important anatomical regions, and may cause dyspnœa or sudden death by pressure upon the trachea or the recurrent laryngeal nerve. Abscesses of the breast, if not opened and drained freely, may lead to extension of the suppuration and to the formation of multiple abscesses. If a mammary abscess is carefully curetted, and is so situated that a counter-opening can be made or that the opening can be made sufficiently large, it may be stuffed with iodoform gauze and all further infection of the gland prevented. Such abscesses heal slowly, however, owing to the discharge of milk into them from the lacteal ducts. The gravest injury may be inflicted upon the medullary cavity of a bone by allowing a case of acute osteomyelitis to run its course without intervention.

It is rare that one regrets a free and early incision; conversely, punctures or small cuts, which are sometimes described as "medical incisions," are likely to produce an increase of all the symptoms, owing to the introduction of fresh sources of infection through the cut surfaces and to the plugging up of the opening by blood-clot.

In abscesses of internal organs, such as empyema, perinephritic abscess, or abscess of the appendix, the operation required is one of major importance. The point of election in these various cases must carefully be selected, and the parts must be divided with the care commensurate with their anatomical importance. In empyema it may be necessary to resect a portion of one or more ribs, partly for the purpose of drainage and partly to allow collapse of the otherwise rigid wall, for it is by contraction of the abscess-walls, as well as by the process of granulation, that an abscess-cavity heals.

In the *spreading forms of suppuration*, or phlegmonous inflammation, the necessity of a prompt intervention on the part of the surgeon is still more strongly called for. The indications in such cases are to reach the micro-organisms at all points where they are growing actively in the tissues, and to attack them with all the resources of antiseptic methods. Their further progress must promptly be arrested. To accomplish this result it is manifestly futile to content one's self with the simple opening of a pus-cavity: such a procedure may aggravate what is already a grave condition. Organisms which have perhaps been held in check by an insufficient supply of oxygen may gain new force or new forms of bacteria may be introduced. At all events, it is not uncommon to find symptoms of septicæmia developing when an acute and deep-seated suppuration has been opened insufficiently.

Free incisions, therefore, are indicated, and pus should relentlessly be followed to the farthest point of the suppurating tissue. When the area involved is an extensive one, it may be preferable to make multiple short incisions, so arranged that drainage may satisfactorily be obtained and that the scar may be so situated as not to interfere with the function of the part. An attempt should be made to remove as much as possible of the necrosed tissues, and great pains should be taken to disinfect all exposed surfaces by free douching with antiseptic washes. After the wounds have been dried they can be packed with iodoform gauze, or rubber drainage-tubes should be inserted freely. The part should then be enveloped in a large antiseptic poultice or in a voluminous dry absorbent dressing. These dressings should be changed frequently, and attempts should be continued to keep down the septic fermentation. The healing of such a pus-cavity or series of cavities must necessarily be slow.

In the early stages of malignant œdema, while a soft œdematous swelling exists, several free incisions through the integuments may suffice to arrest the process. Usually the disease spreads so rapidly that abortive treatment cannot be employed. When the œdema is very extensive Volkmann's method of multiple scarifications has been used with success. This consists in making, with a narrow and sharp-pointed knife, a very large number of small incisions through the skin into the subcutaneous tissue. These incisions should be from 2 to 3 mm. long, and may in some cases amount to several hundred in number. The bleeding soon ceases, and a clear serum presently exudes freely from the various punctures. The flow of serum may be favored by warm douches of 2½ per cent. solution of carbolic acid or by mild solutions of corrosive sublimate. Gentle stroking with the hand from the base to the tip of the extremity also favors the flow. At the end of fifteen minutes the size of the limb will greatly be reduced and many micro-organisms will have been removed from the infected tissue. Disinfection is then brought about by sponging the incisions with antiseptic solutions.

The limb should now be enveloped in iodoform gauze or in some form of antiseptic poultice. Frequent antiseptic baths or permanent irrigation may also be used.

When the disease is further advanced and deeper tissues are involved, this method will not suffice to arrest the process. A more radical treatment is then indicated: the incisions must be longer and deeper; all septic foci must be laid open thoroughly, even if it be necessary to cut down to the bone; the masses of sloughing tissue must be excised, and all the interspaces laid open must be irrigated freely; abscess-cavities should be curetted thoroughly; and the thrombosed veins should be ligatured and excised. In short, no effort should be spared to remove the septic material. Before applying the dressing the limb may be placed for ten or fifteen minutes in a warm solution of corrosive sublimate of 1 : 3000. A dry iodoform dressing should then be applied with firm pressure. If such method of treatment fails to arrest the septic process, the limb should be amputated at a point as near as possible to the healthy tissues. The internal treatment consists in the free use of alcoholic stimulants. Strychnine, nitro-glycerin, and digitalis may be used when the pulse indicates a feeble action of the heart.

The patient should be kept in bed and the limb should be placed in a comfortable position on a pillow. Opium may be given to relieve pain and to ensure rest for the patient. The starting-point of many of these serious types of phlegmonous inflammation is in the hand. It is well to consider some of the commoner forms of suppuration occurring in this locality.

Panaritium (a corruption from paronychia, παρά and ὄνυξ), whitlow, and felon are names used to indicate inflammation situated in the ends of the fingers and in the hand. These inflammations may take their origin either in the skin, in the subcutaneous cellular tissue, in the tendons, in the periosteum, or in the bones and joints.

The infection takes place through some point of injury in the skin. The masses of thickened epidermis on the hands of laboring-men may become bruised or torn or blistered, and the presence of numerous micro-organisms gives conditions favorable for infection. Slight punctured wounds in the hands of carpenters made by splinters of wood may often become very dangerous; the butcher or the cook may become infected by putrid meat through cracks or fissures in the skin. Dissection or operation wounds may be followed by a similar infection. The anatomical arrangement of the connective-tissue fibres on the palmar surface of the hand and fingers is such that they run perpendicularly inward to the palmar fascia or the sheaths of the tendons, and infective material is for this reason readily directed to the deeper parts. The penetration of this fascia produces a division of the abscess into superficial and deep portions, which are united by a narrow sinus. This form, known as the "shirt-stud" abscess, should not be overlooked, as the pus may continue to burrow beneath the fascia even after a superficial opening has been made. When the virus reaches the sheaths of the tendons it spreads rapidly along the channels thus afforded to it. On the dorsum of the hand the subcutaneous fibres run horizontally, and the inflammation therefore remains more superficial and does not so readily involve the tendons.

Panaritium cutaneum, or the cutaneous form of felon, closely resembles a boil. The felon occurs by infection through a wound or an abrasion, and is more likely to be found in the young, whose skin is tender. In older people the skin, being hardened and thickened by work, serves as a protection. The virus penetrates the skin covering the finger-pulp, and makes its way between the vertical bundles into the lobules of fatty tissue lying beneath. The dense fibrous septa prevent the further spreading of the virus and confine it to a limited area, as in the case of a furuncle or boil.

As the minute abscess develops the dense bands of fibres are put upon the stretch. The pulp of the finger is red and painful, and the affected tissues form a dense and well-defined swelling. It is often difficult to determine the exact point of suppuration, but a careful localization of the most painful spot will enable one to determine its locality. If left to itself, the abscess will finally "point," the pus will be discharged, and with it a slough or "core" very similar to that seen in the boil.

Very intense forms of inflammation of this kind may lead to gangrene of the skin or of a portion of the finger. It is well to remember this tendency of the disease in applying carbolic lotions, which have in some recorded cases produced gangrene. Lymphangitis may also be a complication of this form of felon. The disease begins with a chill and considerable fever. Red lines are seen running along the dorsum of the hand and the forearm to the elbow-joint or to the axilla. The lymphatic glands at these two points may become involved in the inflammation, and suppuration may take place.

Panaritium tendinosum occurs most frequently when the subcutaneous form burrows more deeply and the sheath of the tendon becomes infected. The virus is then rapidly carried along the volar aspect of the finger. The tendon-sheaths of the three middle fingers do not extend beyond the heads of the metacarpal bones, while those of the little finger and the thumb are continuous with the bursa of the palm of the hand and extend beneath the annular ligament of the wrist (Fig. 32). For this reason a felon of the thumb or of the little finger is more liable to spread into the palm of the hand, whereas a felon on either of the three middle fingers is more likely to remain confined to those fingers. For these anatomical reasons it is easy to see that the prognosis of a suppurative process involving the tendon-sheath is more unfavorable than that in the superficial variety.

FIG. 32.—Diagram of Tendon-sheaths of the Hand (Tillaux).

The *periosteal form of felon* may arise primarily from a puncture reaching the bone, or secondarily from a suppuration extending downward from a more superficial part. This form of felon occurs most frequently on the terminal phalanx. In the other phalanges the periostitis is usually secondary to a tendo-vaginitis above described. Such a periostitis may lead to necrosis of the phalanx involved or to suppuration of the adjacent joint.

Clinically, it is not usually easy to make a differential diagnosis between the different forms of felon, but the periosteal form may be recognized by the peculiar boring character of the pain and the greater length of time needed for the pus to come to the surface.

The *treatment of a felon* consists in early laying open the inflamed focus. It is rare that such a septic inflammation can be aborted. Early attention to slight injuries about the ends of the fingers, particularly by those who are obliged to come in contact with septic material, may often prevent the establishment of a superficial focus of infection. Every slight scratch and hang-nail should carefully be attended to by the surgeon who desires to keep his hands in proper condition for operation. A rubber cot applied for a few hours will favor a discharge of serum which will float away any poisonous substance that might readily multiply itself if allowed to remain beneath a dried crust or a clot. The frequent use of antiseptics is a great protection which the surgeons of a former generation did not enjoy; consequently "septic fingers" were then much commoner than they are to-day.

If suppuration is established, the pus-cavity should promptly be opened, and the incision should if necessary be carried down to the bone. An incision should also be made promptly in the more severe types of felon before suppuration has been established, as the tension of the parts is thus relieved and the further spread of the virus is prevented. It should, moreover, be the province of the operator to clean out the pus-cavity and to remove all infected tissue, so that the danger of the spreading of the virus may be reduced to a minimum.

Many of these felons can be opened with the assistance of a local anæsthetic, such as cocaine. A rubber tubing should be tied around the root of the finger, and a 2 per cent. solution of cocaine should be injected on either side along the course of the nerves. If the tendon-sheaths are involved and a more extensive operation is required, it is better to etherize the patient. The part should be rendered bloodless, and the burrowing pus should be followed in every direction.

The dressing for these wounds should be in the nature of an antiseptic poultice, for in this way the danger of the retention of any poisonous secretion is greatly diminished. Small areas of bone may be laid bare in felon of the terminal phalanx without necessarily involving the death of the bone. It occasionally happens in a neglected felon, however, that the periosteum of the bone may be dissected completely away from it, and the bone then lies like a foreign body in the centre of an abscess. If a joint is involved, the best that can be hoped for is an ankylosis.

The importance of promptly attending to these abscesses cannot too strongly be urged upon the surgeon, for they involve an organ which is of the utmost importance to all classes of individuals, especially so to those who are dependent upon their hands for their support.

A *palmar abscess* originates in the callosities which form over the metacarpal bones, and which develop as the result of unusual pressure or of friction from work. A fissure in these callosities or the formation of a blister may furnish the entrance-point of an infection. The subcutaneous tissue, when bruised by unusual violence, may also favor such an infection. Palmar abscess may be superficial or may be deep. The latter variety owes its importance to the presence above it of the palmar fascia, which offers a serious obstacle to the escape of pus toward the surface. The pus, therefore, burrows among the sheaths of the tendons, and may find its way between the metacarpal bones to the dorsal surface of the hand. As the abscess forms the tension produced by the pressure upon the palmar fascia is very great, and the pain is correspondingly severe. For the same reason the swelling is not so pronounced as in corresponding inflammation elsewhere. Redness is also less marked on account of the thickened epidermis. There is, however, in many cases an œdematous swelling which may lead to the supposition that the seat of the abscess is in this region.

As has been stated, the infection may occur beneath the palmar fascia secondarily, having worked its way down along the sheath of a tendon from one of the fingers. In severe cases the whole hand may be involved. The tissues then are greatly swollen and the natural furrows of the hand disappear. The fingers are flexed and the hand assumes a claw-like aspect. The suppurative process will not remain long confined to the hand, for the pus readily burrows under the annular ligament, and gives signs of its presence by symptoms of inflammation on the anterior aspect of the wrist. If neglected, the area of suppuration may extend to the region of the muscular tissue of the forearm. There is more or less constitutional disturbance in palmar abscess, according to the extent or the severity of the inflammation.

Careful rules are usually given to enable the operator to avoid the palmar arch. The general rule of following the prolongation of the axes of the fingers and of keeping below the fold of the thumb is usually sufficient. By carefully determining the seat of the pus the knife may be used without fear, and when the pus-cavity has been opened its various ramifications should be followed to their farthest point of extension. A long incision is usually unnecessary. Counter-openings are preferable when the sinus is a long one. In very severe types of inflammation it may be necessary to disregard all anatomical rules and lay open even the annular ligament. Difficulty in controlling hemorrhage rarely occurs, even if the arch is divided. After a prolonged bath in some warm antiseptic solution the hand should be placed in a large antiseptic poultice reaching nearly to the elbow. If the case is a serious one, the patient should be placed in bed and the arm allowed to lie upon a pillow, the hand being slightly elevated. Serious contraction of the fingers may occur, being due to sloughing of the tendons or the formation of cicatricial bands.

Abscesses of the skin comprise pustules, boils, and carbuncles. These affections are caused by invasion of pyogenic cocci from the layers of epidermis down the hair-sheath to various depths in the skin and subcutaneous tissue. When the micro-organisms penetrate the hair-follicles as far as the sebaceous glands and then germinate, there results a *pustule* similar to that seen in acne. It appears as a small nodule in the upper layers of the skin, and varies in size from a pin's head to a pea, according as the seat of the pustules is in the duct of the sweat-gland, or in the glands of the lanugo hairs, or in the large sebaceous glands. The inflammation is usually preceded by an accumulation of sebaceous matter in the gland.

The boil or *furuncle* is caused by invasion of bacteria to a deeper portion of the skin, either through the same route as in the case of the acne pustule or through the sudoriparous gland-ducts. The commoner of the two routes is the former. The seat of the boil in this case is the deeper layers of the cutis and the subcutaneous cellular tissue. The active growth of the bacteria produces in the connective-tissue fibres a coagulation-necrosis, which subsequently forms the "core" of the boil. The part thus destroyed and cast off consists, according to Neumann, of the sebaceous gland and the accompanying hair-follicle. Undoubtedly, the commonest origin of boils is infection through the hair-follicles and sudoriparous gland-ducts of the skin. This was conclusively shown by the well-known experiment of Garré (page 138). Clinical experience confirms this view, and explains the contagiousness of furuncles and the means by which they are communicated to different parts of the skin of the same individual or from one individual to another (acne contagiosa). Athletes undergoing severe training are liable to boils. This tendency is due either to an enfeebled condition of the system or to the bruising of the skin, usually that of the nates, and to infection from soiled clothing saturated with grease and perspiration. Epidemics of furunculosis have, however, occurred where the origin was due not to contagion, but to a mycelium swallowed with certain vegetable substances used as food. It was assumed by Senner that the fungus was conveyed from the intestine into the blood and thence to the skin, as he found threads of the growth in the sloughs cast off from the pus-cavity. This theory would ascribe, in certain cases, the origin of boils to embolism. Among the predisposing causes of boils may be mentioned either the lack of cleanliness of the skin or the excessive use of baths or douches, the presence of organic disease elsewhere, as diabetes, or any lowered state of vitality, as anæmia.

The first symptom of a boil is the appearance of a minute papule situated at the opening of a hair-follicle. Its presence is first noticed through an itching sensation which it causes, there being but slight pain at the time. At first it seems as if the inflamed spot was quite superficial, and that nothing more formidable than an acute pustule would develop. The infiltration of the skin soon becomes more extensive and deeper, and a removal of the projecting hair in no way arrests the inflammatory process.

A small crust forms on the surface of the swelling, and from time to time a minute quantity of pus exudes. If at the end of two or three days the scale is removed, a very fine probe can be introduced for about half an inch into the inflamed mass, and it is now quite evident that the suppuration lies much more deeply than was at first apparent. On palpation the infiltration is found to extend into the subcutaneous tissue, and the swelling may have increased to the size of a pigeon's or a hen's egg.

The pain is usually severe on pressure, and there is always the proverbial soreness associated with this affection. When the boil begins to discharge freely close inspection reveals the presence of a small round opening that extends downward to a pus-cavity containing the slough or "core," which at the end of a week or ten days is usually discharged spontaneously. The opening, which has been considerably distended by the passage of the contents of the cavity, now contracts and the minute abscess heals by granulation. The furuncle developing in the sudoriparous glands is less common: it is more readily recognized on surfaces where there is no hair, as the palm of the hand. It begins with a deep-seated, pulsating pain and a feeling of tension. Sometimes the process seems to be developing beneath the skin. In the cheek it may be felt as a tumor situated between the mucous membrane and the skin. In infants and in young children such boils may be found on the thighs and in parts soiled by urine and fecal matter. Boils may sometimes be complicated by lymphangitis.

Furunculosis is a term applied to those cases where the patient is afflicted with a succession of boils, which appear to come out in crops. The contagion having once been disseminated thoroughly on a susceptible subject, it is a difficult task to destroy the virus or to so change the conditions that the micro-organism will no longer accumulate at certain points. This tendency may continue, notwithstanding treatment, for a year or more in extreme cases.

The *prophylactic treatment of boils* is of great importance. Individuals with a tendency to acne or, to furunculosis should be careful to keep their skin well washed and should frequently change their underclothing. Special attention should be given to disinfection of the nails, and such patients should be cautioned against frequent scratching. When the boil begins to form and is quite superficially situated abortive treatment should be attempted. The simplest and most effective method to abort a boil is to apply with a glass rod or a stick the liquefied crystals of carbolic acid. Equal parts of carbolic acid and tincture of iodine may be applied in the same way. When the process is further advanced, parenchymatous injections of a 3 per cent. solution of carbolic acid may be given with a subcutaneous syringe. In small furuncles only a few drops should be injected; in larger boils nearly a whole syringeful may be necessary. This method is uncertain and painful. A more effective method is to lay the inflamed area open by a crucial incision. In the early stages this operation most effectively arrests further development of the furuncle. It is, however, not applicable to exposed parts where it is desirable to avoid a scar.

The fully-developed boil may be treated by incision and curetting the interior in order to remove the necrosed tissue and the bacteria. This operation should be rendered painless by subcutaneous injection of a 2 per cent. solution of cocaine. The wound should be cleansed with peroxide of hydrogen and filled with a drying powder, such as iodoform, aristol, or dermatol, and be dressed with iodoform or with aseptic gauze. The dressing can be retained with a little cotton soaked in collodion, and can usually be allowed to remain undisturbed for two or three days.

When it is desirable to avoid a scar, the furuncle should be dressed with an antiseptic poultice and the minute pus-cavity be syringed out daily with a weak solution of some antiseptic. In performing this little operation care should be taken not to over-distend the pus-cavity, or the septic process may be made to spread and all the symptoms be aggravated.

When the boil has discharged its core, it may be dressed with cotton held in place by collodion. This dressing is usually the most comfortable in such regions as the neck or the face or the trunk. It possesses the great advantage of establishing an isolation of the boil, so that its secretion cannot contaminate the adjacent hair-follicles. Great care should be taken to keep the surrounding skin in as aseptic a condition as possible, and frequent antiseptic washings should be performed. As a prophylactic measure in case of furunculosis antiseptic baths may be employed. An ounce of sulpho-naphthol in an ordinary bath-tub of warm water furnishes a bath sufficiently antiseptic to remove from the epidermis any excess of bacteria which may there exist.

A great variety of internal treatment has been recommended. The sulphide of calcium is supposed to possess unusual virtues, and is given in doses of $\frac{1}{6}$ gr. three or four times a day. The writer has never seen any satisfactory results from its use. The employment of tonics and nourishing diet, and placing the patient in suitable surroundings, favor such a condition of the system as will enable it to resist a further invasion of the pyogenic bacteria.

Carbuncle is a suppurative and gangrenous inflammation of the skin and the subcutaneous cellular tissue, and begins, like furuncle, on the surface of the skin, but the inflammation spreads downward much deeper into the adjacent structures. The organisms most frequently found in carbuncular pus are the staphylococcus pyogenes aureus and albus. They may be inoculated by the finger-nail in scratching or through small injuries inflicted by the clothing, as the edge of a collar, or through minute blisters. A state of general debility places the tissues in a condition to furnish a favorable soil for the growth of the bacteria. Certain constitutional diseases, such as diabetes, seem frequently to be accompanied by carbuncle. Carbuncle is rarely seen in childhood. It is most frequently observed in persons over forty years of age. A carbuncle is usually situated in the neck and the back, although carbuncular inflammations are occasionally seen upon the face and upon other portions of the body. The term "carbuncular inflammation" is usually employed to convey the idea of a suppurative process developing in a series of separate small foci of pus, and spreading in this way through tissues without any very well defined limits. This application of the term is due to the peculiar appearance of a carbuncle, which seems to develop simultaneously from a number of independent foci. Such, however, is not the case, as the affection begins in very much the same way as a boil, and differs from it chiefly in involving a very much larger area.

The disease begins as a minute papule on the surface of the skin, which usually burns and itches acutely, and the papule may be mistaken for the bite of an insect. It is due to this fact, probably, that flies have often popularly been supposed to be the carriers of the contagion. From this superficial point the area of inflammation gradually enlarges downward and laterally, so that a wedge-shaped portion of the integument becomes involved in the process. When the infection has reached the subcutaneous cellular tissue the disease spreads laterally, the dense fascia covering the muscle preventing deeper infection. Cases are on record, however, where the muscles of the back have become involved in the suppurative process, but these cases are rare.

A glance at the anatomy of that portion of the skin where carbuncle most frequently occurs—namely, that of the upper dorsal region—will serve to explain many of the striking peculiarities of this affection. The skin in this region is extremely thick, probably thicker than at any other portion of the body. It forms a mass of dense fibrous tissue well calculated to sustain burdens or to protect a comparatively defenceless portion of the body. The great bulk of the cutis vera necessitates certain important modifications of contained and contiguous structures. The hair-follicles, being those supporting downy hair only, and therefore shallow, project downward but a short distance into the uppermost layers of this mass of fibre, and there would be no communication with the subcutaneous adipose tissue were it not for oblique columns of fatty tissue which extend upward from below. These fat-columns, or *columnæ adiposæ*, which are found beneath each hair-follicle, are of about the same width as the hair-follicle—perhaps a little broader—and they contain, besides loose connective-tissue, fat-cells, and vessels, the coil of a sweat-gland suspended midway in the

FIG. 33.—Columna Adiposa.

shaft (Fig. 33). There are generally two horizontal branches to this cleft in the skin, and the writer has shown elsewhere how an injection-mass forced in from below may ramify through the whole thickness of the cutis, forming a quite delicate network and marking out the anastomosing system of lymphatic channels. At the point where these columns open into the parts immediately below this dense sheet of cutis is found a broad band of fibrous tissue given off from one side and extending obliquely down into the subcutaneous structures, finally to be attached (tendon-like) to the fascia, beneath which lie the muscles. These fibrous bands, which interlace in various directions, are very different from the delicate "cellular tissue" underlying other portions of the skin, and form a dense network that holds firmly in place the tough hide to which it is attached. In the interstices there is the usual loose connective tissue, which is largely occupied by fat-cells. Students during their dissections become familiar with the toughness of this subcutaneous layer, as does also any surgeon who has once attacked a lipoma in this region with the vain hope that it was going to enucleate easily. It will be observed that the alveoli formed in the meshwork, although having a comparatively limited communication with the neighboring subcutaneous structures, have a tolerably direct, though narrow, medium of communication with the surface through the fat-columns, which, chimney-like, are placed directly above the alveoli.

The characteristic features of the carbuncular swelling, when fully developed, are its broad, flat base, with an oval or a flattened surface raised considerably above the level of the skin. The outline of the tumor is usually circular. The skin is reddened and perforated at several points with holes of considerable size from which pus oozes. A more careful inspection discloses the existence of a large number of minute pustules dotted over the surface of the tumor. The skin is extremely tense and red, and the infiltrated parts have a density unusual in ordinary inflamed tissues. Later, the central portion of the skin is gradually destroyed by the enlargement of the various openings, which fuse together and leave an open crater. The deeper tissues thus exposed appear to be honeycombed with numerous purulent deposits. These peculiar appearances are readily explained by the anatomical structure of the part.

When the deeper tissues become infected and suppurate the pus naturally endeavors to seek an outlet. It cannot spread laterally as easily as in other portions of the body, as the skin is held down firmly on the fascia by the fibrous bands already described. The dense cutis vera also does not yield to the pressure from below. The virus and the pus therefore work from one interspace to another, and thus gradually infiltrate the deep tissues. The pus

FIG. 34.—Infiltration of Columna Adiposa and Subcutaneous Tissue with Pus in Carbuncle.

also makes its way to the surface through points of least resistance, these points being the columnæ adiposæ (Fig. 34). These chimney-like spaces allow a considerable quantity of pus to come to the surface, and where it escapes around the edges of the lanugo hair one of the larger openings is formed. The pus also spreads

FIG. 35.—Diagram of a Carbuncle.

laterally from the column through the lymphatic spaces of the skin, and finally reaches the papillary layers through the perivascular lymph-sheaths. Many of the papillæ become distended with pus, and thus are formed the smaller pustules.

The infiltration and disintegration of the tissues are so complete and the coagulation-necrosis is so extensive that large sloughs form. The centre of the carbuncle thus becomes an open crater, and the dense fibrous meshes of the subcutaneous tissues which constitute the base of the crater are eventually thrown off as sloughs (Fig. 35). As pus accumulates one or more cavities of considerable size form if the skin has not sufficiently melted away to allow of its escape.

Carbuncles may vary greatly in size. A carbuncle is usually from 2 to 3 inches in diameter, about the size of a mandarin orange, but occasionally it may attain an enormous size. It reaches its full development, in the larger varieties, about the end of the second week, and the final healing of the wound, after the sloughs have been cast off, may not be reached for five or six weeks or even longer.

As already stated, the disease does not penetrate the deep fascia, but instances are known in which the suppuration invaded the intermuscular spaces, and Monnier describes a case in which the pus penetrated the spinal canal and caused death from meningitis. In the beginning the parts are painful, but, as the swelling forms slowly, little pain may be experienced by the patient during the further progress of the disease. Paget relates the case of a lady, having a good-sized carbuncle on the back of her neck, who was able to go through with the duties and pleasures of a London season with the carbuncle concealed beneath her hair worn low behind.

The constitutional condition of the patient varies greatly. In the milder cases there may be little or no fever, but large carbuncles are usually associated with considerable cachexia, and the condition of the patient at times becomes critical. The prognosis of the disease is unfavorable when associated with diabetes or when it occurs in persons of advanced years.

Sloughing of the affected tissues is a pronounced feature of carbuncle, and it gives rise to a great loss of substance. Occasionally this process may assume a gangrenous type, and a tendency of the gangrene to spread may become a feature of the case. The writer has seen the entire carbuncle slough away and the gangrene involve a considerable area of the surrounding skin and tissues.

The term "carbuncle" is given to an affection of the upper lip, although most of the characteristic features of a carbuncle are wanting. This is due to the anatomical nature of the part, which differs greatly from the skin of the back. It is, however, like carbuncle, a deep-seated inflammation involving the skin and the subcutaneous tissue. It is usually accompanied by profound constitutional disturbance, and in many cases the prognosis is most unfavorable. This condition is due to the involvement of the rich venous anastomosis with the cerebral sinuses. Thrombosis of the facial vein is a frequent complication, and the suppurative phlebitis may involve the ophthalmic vein, the middle meningeal vein, and may even extend downward to the jugular vein. Death may occur both as a result of meningitis and of pyæmia.

The *treatment of carbuncle* has varied a great deal during the writer's professional experience. Formerly it was the custom to make several crucial incisions through the tumor, thus laying open all its recesses, and then to apply a flaxseed poultice to favor a separation of the sloughs. In cachectic subjects this treatment was often followed by an aggravation of the constitutional symptoms and an extension of the suppuration into the healthy tissues, which were exposed by an unnecessary prolongation of the incisions. A reaction followed this treatment, and one author advised expectant treatment, the sloughs being allowed to suppurate and discharge themselves at leisure.

At the present time the antiseptic treatment has displaced all others. The extent to which antiseptic measures may be carried varies. In milder forms of carbuncle or in subjects who are too feeble to stand any operative measures an antiseptic poultice of cotton, dipped in a weak solution of carbolic acid (1 : 200), may be applied, and such cavities as can easily be reached should be syringed out with an antiseptic wash. The poultice should be renewed frequently, and the surrounding tissue should be washed once or twice daily with a solution of corrosive sublimate (1 : 3000) to protect the sound skin from infection by the pus which is constantly poured over it.

The more radical treatment of removal of the infected tissues is the one that should be employed in the majority of cases. This consists in laying open the carbuncle by crucial incision after preliminary cleansing of the parts, and by thorough removal of the infiltrated parts beneath. This may be done with the curette, with the scissors, or the knife. All infected areas should be excised if possible. In small carbuncles this operation may be performed without pain if the surrounding skin is injected with a 2 per cent. solution of cocaine. The skin may also be removed partially if much infiltrated. Bleeding vessels should be tied if necessary, the parts should freely be dusted with iodoform or washed with peroxide of hydrogen, and the wound be filled with iodoform gauze. Considerable relief from the pain follows this operation, and at the next dressing, which may not be performed for two or three days, the inflammation will have largely disappeared.

In some cases a condition somewhat resembling hospital gangrene prevails: the skin is destroyed and the parts beneath are covered with extensive sloughs. The edges of this crater are reddened and infiltrated, and frequently undermined by the gangrene. The circulation appears to be too feeble to furnish sufficient fluid to throw off the sloughs. Under these circumstances the patient should be etherized and the gangrenous tissue should be removed with a sharp spoon or with scissors, and the edges of the wound should fully be laid open by incisions through the skin. The thermo-cautery should then be applied over the whole infected surface.

The most radical treatment consists in total excision of the carbuncle. This operation has been advised in cases of severe constitutional disturbance when the strength of the patient is insufficient to produce any healthy reaction at the seat of the disease, or in old people in the early stages of the disease when it is desired to spare them the dangers of septic infection. A circular incision should be made around the edge of the infected portion of the skin, and all diseased tissue should rapidly be removed. As this method involves a considerable loss of blood, it would be preferable to make the skin incisions only with the knife and to finish the operation with the actual cautery, or to perform the whole operation with the cautery knife, which may be done without the loss of a drop of blood. The effect of the removal of such a source of contagion is immediate. The fever and delirium disappear, the pain is greatly relieved, and the patient obtains refreshing sleep.

Carbuncle of the lip may occasionally run a mild course, but in a typical case the symptoms are very grave, and the treatment should be prompt and heroic. It is not sufficient to content one's self with one or more incisions. The infected area should be extirpated. Winiwarter reports two cases in which he approached the carbuncle through the mucous membrane, and, having excised all diseased tissue, filled the cavity thus made with iodoform gauze. These cases made a good recovery without visible scars.

In the severer form of carbuncle the constitutional disturbance needs careful attention. The patients, who are frequently aged and infirm subjects, should be confined to the bed. The diet should be digestible and highly nutritious, and should be given in small quantities at frequent intervals. Alcohol should be administered with a free hand, but the patient should be watched to see if the use of stimulants causes flushing. Opium in some form may be needed to relieve pain and ensure repose, and if the heart's action be feeble digitalis may be given in moderate doses. The chief reliance in these cases should be, however, on nourishing diet and alcoholic stimulants.

4. Ulcer.

An *ulcer* is a solution in continuity of the skin or the mucous membrane which shows no tendency to heal. An ulcer has been defined as molecular death of the part: it owes its existence, in fact, to an excess in action of the retrograde changes over those of repair. In this respect it differs from an open granulating wound, which possesses a tendency to heal. The latter may, however, become an ulcer at any time if the granulations begin to break down. The process is closely allied to that known as *necrosis* or *gangrene*.

Ulcers are classified at the present time chiefly according to their mode of origin. A large number of ulcers result from infectious disease, such as syphilis, tubercle, leprosy, and glanders; perhaps, also, cancer. The non-infectious ulcers are preceded and accompanied by a chronic inflammatory process in the tissues in which they develop. The loss of substance may be the result of the inflammatory process, or it may be the primary condition around which the chronic inflammation has developed itself. Among the local causes for the development of an ulcer is the tendency to degenerative processes in the inflamed tissue or impairment of the circulation. Thus, a local anæmia may be produced as the result of obliterative changes in the walls of arteries or impairment of the venous circulation. Trophic disturbances may be caused by an impairment of the innervation of a certain portion of the body. Local irritation, with breaking down of tissue, may be caused by friction or by pressure. Mechanical obstacles to the healing of a wound must also be regarded as a cause of ulcer.

The anatomical characteristics of an ulcer are determined by the nature of the ulcerated surface and its margins. The ulcerated surface presents a great variety of conditions according to the influences to which it has been subjected. In freshly-formed ulcers there is an inflammatory exudation mingled with fragments of broken-down tissue or tissue in a state of coagulation-necrosis. Beneath this tissue lies a layer of cells forming what is known as *granulation tissue.* The cells of which this layer is composed are largely polynucleated leucocytes and epithelioid cells, with comparatively little intercellular substance. A rich capillary network of blood-vessels runs through this tissue and sends branches toward the surface. The tissue underlying this somewhat superficial layer of cells contains a greater quantity of intercellular substance or many fusiform cells. Often this tissue is made up largely of an œdematous fibrous tissue with small clusters of cells considerable distances apart. Below this there is usually found some of the fibrous tissues of the deep layers of the skin. The granulation tissue is soft and succulent, and may easily be scraped away with a curette. The tissue below is much denser, and appears as a white fibrous layer which shuts off the granulations from the surrounding healthy tissues.

The edges of the ulcer consist of the surrounding skin, which has been more or less altered by inflammatory changes. There is usually some thickening of the skin, which is consequently raised

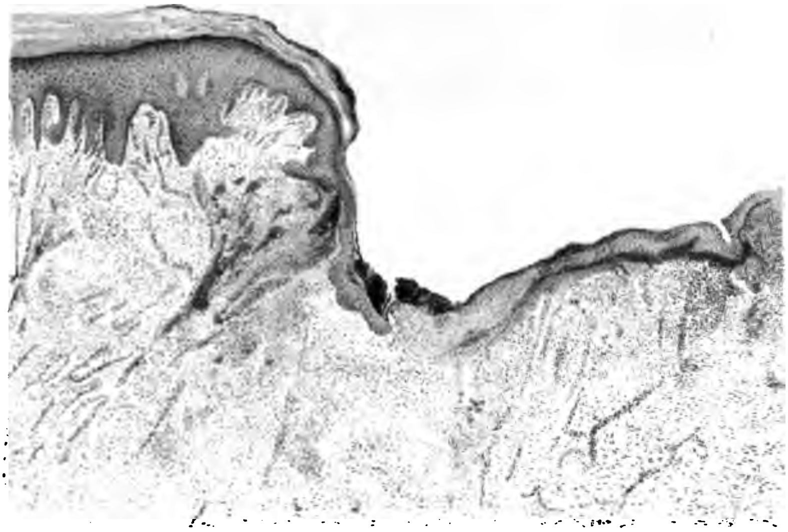

FIG. 36.—Ulcer of Leg.

above the surface of the ulcer. The papillæ are in these cases somewhat hypertrophied. In and below them we find numerous leucocytes and epithelioid and fusiform cells in various stages of development. In the deeper layers of the rete mucosum and in the papillary layers of the skin in old ulcers masses of blood-pigment are seen (Fig. 36). The margins of the ulcer are frequently on a level with the ulcerated surface; sometimes they are undermined by the granulation tissue. Under these circumstances the skin is red and infiltrated, and often has a bluish tinge, due to the feeble nature of the circulation. The borders of the ulcer may become firmly adherent to the deeper parts, particularly bone or periosteum.

The non-infective ulcers are classified according to their mode of origin or according to certain characteristic peculiarities they possess. Among the numerous varieties described in medical literature may be mentioned the inflammatory ulcer, the callous or atonic ulcer, the varicose ulcer, the neuroparalytic or perforating ulcer, the phagedenic or gangrenous ulcer, and the erethistic or irritable ulcer.

The *inflammatory ulcer* is caused by bruising or friction of a part, and is traumatic in origin. Inflammatory ulcers are more frequently seen upon the legs, as the persistence of the ulcer is due to the mechanical condition of the circulation, which favors a stagnation of the blood in the part, in consequence of which the efforts at repair are more feeble. These ulcers may also be caused by burns or by frost-bites or by the action of chemical substances.

The commonest form of ulcer seen by the surgeon is the *varicose ulcer*, which is situated on the shin, usually at the junction of the middle and lower thirds. Its origin is readily recognized in most cases by the varicose veins seen running beneath it and from its upper margins to the inner border of the popliteal space. The cause of the ulceration is a passive hyperæmia, in consequence of which stagnation of the blood takes place in the smaller veins and capillaries, and the surrounding tissues become saturated with a thin serum which oozes through their walls. This is the cause of the œdema which, in a greater or lesser degree, accompanies the disease. With the serum there is an exudation of red corpuscles, producing an extensive pigmentation of the skin, which usually precedes or accompanies the stage of ulceration. The nutrition of the part being thus enfeebled, a slight blow will cause an abrasion of the epidermis, and the minute wound thus made will gradually develop into an ulcer of considerable size, or a minute slough may be caused by a thrombosis of one of the small superficial veins. With the formation of a wound infection takes place by bacteria invading the exposed surfaces, and the element of inflammation is thus introduced. The surrounding parts are now infiltrated with leucocytes, and are further softened by a continuation of the inflammatory process. In neglected ulcers the amount of inflammation may be great and the limb may become swollen, tense, and excessively painful. Phlebitis may occasionally become a complication of the process.

Ulceration from pressure may occur in a manner somewhat similar to that by which decubitus or bed-sore is produced. It differs, however, from decubitus in the absence of a slough. The principal seat of these ulcers is in the sole of the foot, although they may be found on prominent spots about the inferior extremities as the result of pressure from splints. The pressure is not severe enough to produce stasis and death of the part, but as the result of continuous pressure the epidermis thickens and a callosity forms, which, acting as a foreign body, produces friction upon the true skin below, causing inflammation; eventually suppuration takes place beneath the thickened mass of epidermis. A small ulcer is thus developed, which is surrounded by raised edges consisting of a greatly hypertrophied layer of epidermis. The rigidity of the parts and the low vitality of the tissues at the base of the ulcer prevent cicatrization.

Ulcers are particularly liable to develop in paralyzed parts. They may be caused by inflammatory processes which readily occur in such localities or as the result of pressure. The insensibility of the skin and the lack of muscular action allow pressure to remain constant on a given spot. Absence of muscular contraction also favors a stagnation of the venous blood in the tissues, which predisposes to ulceration.

The so-called *mal perforant*, which occurs upon the sole of the foot, appears as a sharply-cut circular ulcer with surrounding thickened edges, often almost completely shut in by the overhanging borders of epidermis. It is found most frequently beneath the metatarso-phalangeal articulation of the great toe, but may be found on any part of the sole of the foot which is subjected to the most pressure in any particular case. This form of ulcer has been supposed to be associated with disturbances of nutrition in the nervous system. These disturbances may be due to a local affection of the peripheral nerves, accompanied with inflammatory or degenerative changes, or to some central lesion. It has been found frequently associated with locomotor ataxia. This supposed association with certain trophic nerve-disturbances owes its origin partly to the fact that the borders of the ulcer are anæsthetic. A pin may be introduced for some distance into the adjacent skin without causing pain. According to Winiwarter, the nerve lesion is not the direct cause of these ulcers, the exciting cause being the local irritation produced by pressure or by friction. No distinction should be made between those of a neurotic and those of a non-neurotic origin. It is, in fact, an ulcer due to pressure such as has already been described.

A microscopical examination of a perforating ulcer shows in the ulcerating surface masses of hyaline material enclosing red blood-corpuscles and molecular detritus, and very few cells. The surrounding skin is much sclerosed and the papillæ are usually hypertrophied, and above them are piled up enormous layers of epidermis.

If pressure is continued for a long time upon the ulcer, the inflammation and suppuration spread, and the adjacent joint of a toe may become involved, and necrosis of the bone may result. This process is not to be mistaken for senile ulceration or gangrene, which is found upon the toes and foot, though usually not on the plantar surface.

French surgeons recommend amputation for *mal perforant*, and the writer has seen several cases treated in this way. Usually, however, rest in bed with local treatment by antiseptic poultices suffices to heal the ulcer. Careful removal of the rigid margins and curetting the indolent surface of the ulcer will place it in a condition favorable for repair.

Similar ulcers are sometimes seen upon the feet of patients afflicted with anæsthetic leprosy, and are in such cases probably —in part at least—of bacterial origin. The writer amputated the foot of a patient for this disease. The foot was misshapen and greatly clubbed, and upon the most dependent point an ulcer existed which seemed largely due to pressure.

Ulcers may be classified according to certain changes or complications which occur during their existence. An inflamed ulcer is one in which the base and surrounding parts are more or less acutely inflamed. The ulcerated surface is intensely red, bleeds easily, and secretes pus freely. It may be at times covered with sloughs or croupous membrane. The borders are swollen, and the surrounding skin is often tense and shiny and excessively tender. These conditions are caused by neglect, by application of irritating substances, or by contact with acrid secretions. Ulcers in this condition often become very painful.

Erethistic ulcer is one in which great sensitiveness persists and is hard to relieve. The ulcerated surface has the appearance of a tissue which is not in an active state of repair. There is no tendency of the edges to cicatrize: they present rather the appearance of being bitten out. The slightest touch is often excruciatingly painful. Painful ulcers are often found in the neighborhood of very sensitive parts, as the anus. The cause of the great sensitiveness has been ascribed to an unusual thinness of the granulation tissue. It is often due to pronounced anæmia following loss of blood or to severe disease, and disappears with a return to the normal condition of nutrition (Winiwarter).

The *fungous ulcer* is caused by an excessive growth of granulations. This growth is due to an abundant blood-supply without any disposition on the part of the edges to approximate themselves. They are found upon very vascular parts where the epidermis is thick, as on the hands and the feet. Such a condition of the granulation is popularly known as "proud flesh," which is supposed to be an obstacle to the healing process. It often happens in wounds of the hands or of the feet that a luxuriant growth of granulations will form a little tumor projecting above the somewhat rigid edges of the skin. The epidermis pushes its way into the granulations and a mushroom-like tumor is formed with a small pedicle. If the tumor is cut off, an arteriole of considerable size is found around which new tissue is rapidly formed, and the tumor grows again before the sluggish epidermis succeeds in closing the wound. Such granulation tumors must be shaved off even with the surface, and the small opening left should be cauterized with a stick of nitrate of silver, so as to destroy the nutrient artery. Compression should then be applied and the ulcer will readily heal. Fungous granulations often protrude from the mouths of fistulæ, particularly those leading to tuberculous abscesses or to a foreign body.

Hemorrhagic ulcers are most frequently seen in scurvy. The ulcerated surface is a livid blue, and the granulations readily break down. A vicarious hemorrhage is sometimes seen in cases in which there has been a suppression of the menses or an arrest of bleeding from hemorrhoids (Winiwarter).

Torpid ulcers are seen in individuals suffering from the cachexia of an acute or a chronic disease, in consequence of which there is a diminished blood-supply to the part. The granulations are pale and the secretion is thin and watery.

A *callous ulcer* is one which has existed without material change in size for a long period. The surface is dirty and it secretes a thin muco-purulent material. The edges are raised considerably above the surface, and the skin for some distance around is indurated and immovable. Old varicose ulcers often present this type.

Phagedenic ulcers are those which spread rapidly with symptoms of great local irritation. They are seen in epidemics of gangrene or in ulcers which have been treated by irritating applications. A chancre may occasionally become phagedenic, and when in this condition it is an unusually obstinate affection. Antiseptic lotions and the application of iodoform in powder, with tonic treatment, will usually arrest the process. If the miserable, broken-down individuals who are usually the subjects of this form of ulcer can be placed in favorable surroundings, the disease will readily yield to treatment.

The treatment of ulcers in general consists primarily in the elevation of the part, so that the circulation, which is an important factor in their development, may properly be regulated. The passive hyperæmia which exists, particularly in the case of varicose veins, must be relieved, in order that the parts may return to their natural condition and that they may thus be enabled to carry on the process of repair. A neglected ulcer is usually in a very foul condition, owing to the decomposition of pus and sloughs confined beneath scabs and to the presence of macerated epidermis containing a great variety of bacteria.

An antiseptic poultice of carbolic acid or of phenyl (1 : 250), applied to the limb after the patient has been placed in a bed, usually suffices, with frequent antiseptic washings, to remove all odor in a few days: the poultice eventually cleans the wound thoroughly and enables the parts to throw out healthy granulations. Among cleansing washes may be mentioned peroxide of hydrogen, weak solutions of permanganate of potash of a strength slightly to redden water, chlorinated soda, and carbolic acid, all of which owe their virtue in part to their ability to penetrate greasy substances. A weak wash of tincture of iodine may also be used to advantage, particularly if there is any reason to suspect the presence of tubercle. If it is desired to apply a dry dressing, iodoform or aristol may be used if the odor is strong. Dermatol powder has a soothing effect, and has the advantage of being odorless. In mild types of ulcer pure zinc ointment is a useful dressing, as it forms a protective layer which cannot easily be removed.

Erethistic or painful ulcers are usually not amenable to any form of dressing. Poultices are complained of bitterly as heating and "drawing." A perfectly neutral material, like vaseline, answers best on such ulcers. An ointment composed of hydrochlorate of cocaine, 12 grains to the ounce, applied once daily, gave great relief in the writer's experience. A protective of gutta-percha tissue is often superior to any other dressing in cases of erethistic ulcers.

Indolent ulcers are often stimulated by the application of balsam of copaiba or balsam of Peru on charpie. Tincture of myrrh, 1 drachm to the ounce of water, applied on charpie, has a very tonic effect upon the granulations. The patient should be encouraged in cases of ulcers of the lower extremities to keep the limb elevated. If possible, he should remain in bed, and he should be impressed with the importance of absolute rest to the part.

When it is necessary to treat the case as an ambulating one, the passive hyperæmia may be relieved by pressure by bandage or by adhesive plaster. The ulcer should then be strapped with narrow overlapping strips of diachylon or with rubber plaster. A flannel bandage, cut bias and about 4 inches wide, should then be applied from the toes to the knee. The plaster may be allowed to remain two or three days; the pus which collects beneath the plaster during this time is, in favorable cases, of an unirritating character and serves the purposes of a moist dressing. The rubber bandage can be used successfully for the same purpose, as rubber is usually unirritating to granulating surfaces. The patient may be instructed in its application, and the bandage may be removed once or twice daily for the purpose of washing the ulcerated surface. The rubber bandage is, however, an uncomfortable and inelegant mode of treatment, being suitable only for laboring people who cannot spare the time for more elaborate treatment.

Many ulcers owe their inability to heal to the firm adhesion of the surrounding skin to the parts beneath. Much benefit has been obtained by lateral incisions, which release the edges of the ulcer and allow cicatrization to go on. By far the most effective of operative procedures is skin-grafting after the method of Thiersch. This operation is so simple that it can readily be performed by any practitioner. It consists in the removal of the granulating surface by scraping with a curette or by shaving with an amputating knife. The parts should be washed thoroughly, and all antiseptic agents should be removed with boiled water or with a sterilized salt solution, .6 per cent. Thin shavings of skin should be removed from the thigh of the patient, the parts having also been carefully washed beforehand. The portions removed should be about 1 inch in width and from 2 to 6 inches in length. They should be so laid upon the re-freshened surface of the ulcer as to overlap one another slightly, and should extend a short distance beyond the margin of the wound. Thin strips of gutta-percha tissue or of thin rubber should be laid over grafts, and an aseptic dressing should then be applied. The dressing should be renewed in about three days. If the grafts have adhered, they will be found to have a slightly pinkish tinge. Too long use of the rubber tissue, owing to the macerating influence, endangers the life of the grafts.

Small ulcers may be grafted in this way without etherization. In such cases a subcutaneous injection of cocaine will be needed to produce local anæsthesia. In large ulcers great attention to all details is needed to ensure success, but in small ulcers the operation may be performed successfully without any elaborate preparations. In the case of ulcer upon the leg the patient should not be allowed to walk for several weeks after the operation, as the cicatricial tissue will break down and the ulcer will reappear if the limb is placed in a dependent position at too early a date.

5. Fistulæ.

A fistula may be defined as an abnormal opening into a normal cavity or organ or as a long, narrow channel indisposed to heal. In the former case the wound may have healed, but the hole remains, through which the normal secretions escape. A fistula which communicates with a suppurating cavity resembles in its nature an ulcer, and like that affection may be the result of the failure of an abscess to heal. It is, in fact, a cylindrical ulcer, and its walls resemble, histologically, the surface of an ulcer. It is surrounded by a mass of more or less indurated and inflamed tissue, and its surface consists of a layer of granulation tissue which shows all the varieties of appearance seen in ulcers.

A fistula may be caused by the anatomical relations of the part or by the peculiar shape of the wound or abscess-cavity. It may be due to the escape of physiological secretions or excretions, such as saliva or fæces, and it may also be due to the presence of a foreign body or a sequestrum or fragment of sloughing tendon.

After laparotomy or extirpation of a tumor, like that of the thyroid gland, where numerous ligatures are used, a fistulous opening frequently remains, leading to a ligature which has not been enclosed in the cicatricial tissue.

When pus has burrowed for a considerable distance beneath the skin, and a long and narrow granulating surface has been established, the mere shape of the cavity is in itself an obstacle to cicatrization, as the secretions have no opportunity to escape. The presence of a specific virus like that of tubercle or cancer is also an adequate cause for the permanence of a fistulous opening.

The *treatment* of the fistulous ulcer consists in laying it open, so that it may be converted into a wound with a wide opening that may heal from the bottom, or in the removal of the foreign body which prevents cicatrization, or in the application of medicated substances to its inner surface.

When a fistula is surrounded by inflamed and indurated tissue the condition is usually due to contained secretions which have been prevented from escaping by imperfect efforts at cicatrization. In such cases poultices or soothing applications should be employed to allay all irritation before any attempt is made to favor repair.

The fistulous opening must then be enlarged, and the canal must be made, if possible, an open wound, to which a dressing may be applied throughout its whole surface. All foreign bodies must of course be removed, and secretions of pus be allowed full vent. Sinuses which run subcutaneously should be laid open freely and the various ramifications followed to their extremities. The surface of the fistula should then be curetted thoroughly, so that healthy granulations may replace the indolent tissue which existed there.

Small fistulæ can completely be extirpated and the healthy tissue can be brought together and made to heal by first intention. With careful antiseptic precautions this method may be carried out in cases of *fistula in ano*, which are usually tubercular in origin. In cases in which neither incision nor excision are applicable the thermo-cautery may be used with success.

Medicated injections that may be used to exert a healing influence upon the walls of a fistula are numerous. Solutions of carbolic acid (1 : 200) or phenyl (1 : 250) may be employed for the purpose of disinfection. Corrosive sublimate is not so useful for this purpose, owing to its inability to penetrate greasy substances and its conversion into an inert aluminate.

If there is reason to suspect tuberculosis, a weak solution of tincture of iodine, of about the color of sherry wine, is an efficient application. A 10 per cent. emulsion of iodoform in glycerin, and Krause's emulsion, which also contains gum arabic and carbolic acid, are valuable remedies in tuberculous fistulæ. Peroxide of hydrogen may be employed as a cleansing agent for fistulous ulcers.

A very weak solution of nitric acid (1 drop to the ounce) is often effective in healing small fistulæ connecting with bone. The success of this treatment may be due to the antibacterial virtues of the acid or to its solvent action in the carious or necrotic bone.

Attention should be given in all cases to the general condition of the patient and his surroundings. A chronic fistula has often been known to heal after some acute intercurrent disease, such as scarlet fever. A thorough change in the habits of life may also bring about the same result. Tonics and non-irritating diet would be valuable adjuncts to such treatment.

VIII. INFECTIVE INFLAMMATION.

ACUTE OSTEOMYELITIS.

ACUTE OSTEOMYELITIS is a disease which furnishes our hospitals with the greater portion of the cases of necrosis that students are accustomed to see operated upon in the amphitheatre, but, although so common, it has escaped general attention from surgeons in its earlier stages. It is only the sequelæ of the disease that one usually has an opportunity to study. The disease-process itself runs an acute course, and at times presents a group of symptoms of so grave and so obscure a character that its true nature is frequently overlooked. It has often been mistaken for typhoid fever or for acute rheumatism; hence such names as "bone typhoid," etc. The pathological anatomy of the disease has only been interpreted correctly within comparatively recent years. The older surgeons who had occasion to open the abscesses that formed in the early stages of this affection found the collection of pus between the periosteum and bone, and concluded that they had to deal with a suppurative periostitis; the same mistake is frequently made at the present time. Now that more is known about the etiology of the disease, and the fact is recognized that these acute bone-suppurations are caused by the growth of the pyogenic cocci, whether they arise in the medulla, the spongy or the cortical bone, or the periosteum, and that frequently all these portions of the bone are involved, it seems important to discard a nomenclature which gives but an imperfect idea of the nature of the disease, and to employ the more comprehensive term *osteomyelitis.*

This form of bone-inflammation is seen most frequently in childhood. A young lad bruises or sprains his leg during play or exposes himself for an unusual length of time to wet and cold. Presently acute febrile symptoms usher in an attack of illness, and it is soon discovered that the knee-joint is apparently involved in a rheumatic inflammation. A more careful examination shows the seat of the morbid process to exist in the lower portion of the femur or in the upper end of the tibia. The local symptoms become more marked, and the constitutional disturbance may be so great that in exceptional cases the patient succumbs in a few days to symptoms of septicæmia. In the majority of cases the formation of an abscess is soon apparent, and with the outlet of the pus the general symptoms subside. The wound thus made does not heal, and after months of waiting the patient applies to a surgeon, who finds a mass of dead bone at the bottom of the fistulous tract. Such a condition, if not relieved by surgical interference, may last a lifetime, or the patient may die eventually from the effects of prolonged suppuration.

The etiology of this disease is now thoroughly understood, a large number of observers having identified the pyogenic cocci as the organisms which are found in the pus from these bone-abscesses.

Pasteur was one of the first to recognize the fact that this inflammation of bone was caused by a micrococcus, and Ogston found pyogenic cocci in the pus of a case of osteomyelitis. At one time in the early history of these experiments in France and Germany it was supposed that a specific organism was the cause of the disease, but later studies have shown this theory to be untenable. Rosenbach made one of the first systematic studies of the bacterial origin of the disease, and in fifteen cases of osteomyelitis he found the staphylococcus fourteen times—once with the albus and once with the streptococcus—and in the fifteenth case he found the albus alone. He succeeded in imitating successfully Kocher's experiment, which consisted in the injection of pus into the vein of an animal after fracture of one of its bones, thus producing suppuration of the bone. Rosenbach's inoculations were made with the pure culture of the aureus, and suppuration was invariably produced if the bone had previously been fractured.

Among the most elaborate experiments are those of Courmont and Jaboulay. These observers injected two drops of a culture of the staphylococcus into the veins of a young rabbit, which was taken ill in forty-eight hours with swelling of both knees. Death occurred at the end of eight days. Abscesses were found in both kidneys and in the muscles, particularly those of the heart. Sero-purulent arthritis of the knee-joint was also found. Congestion in the epiphyseal region of the lower extremity of the corresponding thigh was observed. In similar cases evidences of periostitis were seen, and sequestra were found near the epiphyseal line. Pus from an abscess of the arm produced, on injection, medullary abscesses in rabbits a few weeks old. Streptococci taken from a case of puerperal septicæmia produced abscesses in the ends of the long bones of rabbits near the epiphyseal cartilages.

These observers conclude that this disease may be caused by both the staphylococcus and the streptococcus. The staphylococcus attacks the juxta-epiphyseal regions, producing a periostitis with necrosis and sometimes inflammation of the joint. It reproduces pretty accurately the juxta-epiphyseal osteo-periostitis of man, whereas the streptococcus seems to attack the medullary cavity—usually near the juxta-epiphyseal line—and produces a more diffuse suppuration.

Ullmann states as the result of a large number of carefully-conducted experiments that he was unable to produce the disease by injections of the virus unless some kind of injury had previously been inflicted upon the bone. The application of a temporary ligature to a rabbit's leg for from twelve to fourteen hours was found to cause certain changes in the marrow of the bones, particularly extravasations and circumscribed hemorrhages, which were sufficient to predispose these parts to infection. Ullmann considers the staphylococcus as the usual cause of osteomyelitis.

Kraske obtained in two out of five cases of osteomyelitis a pure culture of the aureus. In three cases numerous organisms were seen, among them being two forms of bacilli. Those cases in which several kinds of bacteria were found appeared to be of a more malignant type, as when a mixed infection of streptococci and bacilli was found.

Kraske points out that many cases closely resemble pyæmia in their origin. It often happens that an osteomyelitis may originate from an abscess of the skin or of the subcutaneous connective tissue which has already healed. This author suggests that the tonsil may also be the point of entrance of the virus. He doubts the possibility of an invasion through the intestinal tract, but thinks that the respiratory organs may offer an entrance to the bacteria. It is quite probable that the virus often enters through excoriations or bruises or small wounds in the skin. The recurrent forms seen in adult life are explained by Kraske as due to the presence of spores which have remained for a long time encapsuled, and have eventually been freed from their long imprisonment. It is possible, however, that a second attack may be due to a new infection. The first attack appears to create a predisposition to a second one. The exanthemata produce a condition also favorable to the occurrence of osteomyelitis by manuring the soil, as it were, for the growth of the pyogenic cocci. Park showed that abscesses of bone and the periosteum may be caused, in a certain number of cases, by a mixed infection of the pyogenic cocci with the typhoid bacilli or with the bacilli of tuberculosis, and possibly also with the virus of syphilis. Changes in the bone-marrow are set up in a large number of infectious diseases, such as typhus, typhoid, or intermittent fever, and suppurative changes can easily be established in the bone under these circumstances.

According to some observers, the typhoid bacillus is capable of producing suppuration. Fränkel found only the typhoid bacilli in an abscess of the abdominal wall after typhoid fever, but Park found the staphylococcus with the typhoid bacilli under similar circumstances. These bacilli have been detected in subperiosteal abscesses by Ebermaier, who considers that they reach the periosteum from the medullary part of the bone through the Haversian canals. Park observed only the pyogenic cocci in post-scarlatinal abscesses: whether a specific organism of the disease is also present can only be determined after the nature of scarlatinal virus is understood. It is possible that the specific organisms of certain diseases may become localized elsewhere at first, and, when the system is debilitated by the effects of the disease thus produced, bring about suppuration in the bones.

Koplik found pure cultures of the streptococcus in several cases of osteomyelitis in infants, but, as this author states, all the cases belonged to the so-called "septico-pyæmic" class. Cultures of these organisms injected into the circulation of healthy rabbits caused an inflammation of the joints of the posterior extremities, terminating in suppuration. The medulla of the bones corresponding to these joints was invaded with streptococci. These experiments suggest the theory that cases of multiple osteomyelitis are due to the agency of the streptococcus.

A glance at the *anatomy of the ends of the long bones* throws some light upon the selection of this particular point as the seat of suppurative disease. This region is called by Ollier "the zone of election of pathological processes." Near the epiphyseal cartilage, which separates the diaphysis or shaft from the epiphysis, there exists in growing bones a newly-formed spongy tissue, very vascular and connected with the cartilage by a spongy layer of tissue, which is not yet bone, but which does not possess a cartilaginous structure. It is in this portion of the organ that the most active changes take place during the period of growth. The medullary substance is very vascular at this point: it is red and without fatty tissue. It communicates with the medullary canal and with the periosteum by a number of vascular channels. The epiphyseal cartilage itself is intimately blended with the periosteum. The diaphyseal side of the cartilage produces much more bone than is found on its epiphyseal margin. There is also an active growth of bone in the periosteum, and it is in these regions and in the medullary canal that the inflammatory processes originate. The question has been asked whether the disease begins at that end of the bone toward which the nutrient artery is directed. If this were the case, the fact would suggest for the inflammation an embolic origin which probably does not occur. In the femur the artery is directed upward, yet the lower portion of the bone is most frequently affected. The reverse conditions exist in the tibia.

The compact bone is never primarily affected; in fact, the bony tissue is of minor importance in this form of inflammation. As might be expected, the disease is most frequently seen during the period of active growth in the bone. It is much less frequently seen in women than in men, but this is probably due to the fact that the former are less exposed to injury.

Among other *predisposing causes* are those which bring about an enfeebled condition of the system, such as unhealthy surroundings and poor food or long exposure and fatigue. In enfeebled individuals the tissues are less resistant to the action of bacteria. Ullmann was able to produce the disease experimentally, by injection, in animals suffering from a considerable loss of blood, and he found that in these cases no previous injury of the bone was necessary.

FIG. 37.—Point of Origin of Suppuration in Osteomyelitis.

Some slight injury, such as a blow, not unfrequently a kick, given to a boy by his playmate, or a sprain, is sufficient to produce in this delicate tissue, with its rich vascular supply, a bruising of the vessels and an effusion of blood—at all events, a certain amount of damage which temporarily interferes with the nutrition of the part. Minute fractures of the bony trabeculæ not unfrequently are found after such injuries. At these points the bacteria which may be circulating in the blood move in a comparatively confined vascular area, and readily find lodgment in the bruised tissues or the blood-clots. Where the *pathological process* originates the unyielding nature of the tissues favors, at times, a rapid spread of the inflammation through the Haversian canals, through which the blood-vessels pass. At other times the inflammation remains for a period localized (Fig. 37).

The red color of the medulla of youth is preserved in the bones of the trunk and the head during growth and in adult life, but it is lost in the medulla of the bones of the extremities, where the tissue is of a yellow hue, due to the presence of fatty tissue. In osteomyelitis this tissue becomes reddened, but unlike the normal medullary tint, and there is an increase in the consistency of the tissue. The fat-cells disappear, and the part becomes infiltrated with granulation-cells and some red corpuscles. There is, in fact, a great increase in the number of leucocytes and of cells containing red masses and pigment-granules, and an increase also in the number of leucocytes throughout the organism, so that an "inflammatory leukæmia" has been said to exist. The spleen may be enlarged, and hemorrhagic exudations are often found in the serous cavities. Ullmann found, in dogs with osteomyelitis, that the leucocytes were increased from four- to sixfold. The inflammatory exudation is not diffuse, however, but collects at numerous foci, which give to the part a mottled appearance due to local congestions and to extravasations of blood. As these foci soften they turn yellowish-gray or dark red according to the amount of blood or pus they contain. The bone, on section, shows collections of pus or of spongy tissue infiltrated with pus. The numerous abscesses are varied in form and size, and are often arranged in rows near the epiphyseal cartilage. As soon as suppuration is established there forms a line of granulations which separates the diseased from the healthy tissue. New tissue is formed both in the medulla and in the periosteum, containing many osteoblasts, which are capable of producing new bone. An absorption of tissue takes place at these points, thus separating the dead from the living bone.

As the amount of pus increases, it either spreads by infiltration along the interior of the shaft of the bone or it works its way through some of the natural channels (as the Haversian canals) to the surface, and accumulates beneath the periosteum, separating it from the bone (Fig. 38). When the pus breaks through this obstruction it burrows next between the muscles, and it may form one or more distinct abscesses. The pus which they contain is at first of a brownish color, occasionally has a very foul odor, and is accompanied by the discharge of extensive sloughs. It frequently contains innumerable drops of medullary fat, which is said to be quite a characteristic feature of these abscesses, and therefore to possess a certain diagnostic value. This fat is due to increased pressure in the medullary cavity, which forces the fat-drops through the Haversian canals.

In many cases the epiphyseal cartilage remains intact through all this inflammation, and offers an effective barrier against the spread of the disease toward the joint. In some cases, however, it is broken through and disappears, and the disease attacks the epiphysis. One joint may be affected either by a direct extension of the pus in this way through the bone or by the more circuitous route from abscesses which have perforated the periosteum and eventually have pushed their way through the capsule. As the epiphyseal cartilage is absent in the adult, the joint is more likely to be affected at this period of life.

FIG. 38.—Extension of Suppuration in Osteomyelitis.

The effect of this acute suppurative process is to cause *necrosis* or death of the bone. When the shaft of the bone is involved in the ordinary way, a few fine, needle-like particles of dead bone may be found in the medullary canal during the first few days of the process. Later, larger fragments may be found to have separated, either as exfoliations from the surface or as fragments from the denser portions of the medullary bone. When the pus reaches the periosteum, it may burrow for a long distance beneath it, and a large portion of the shaft may thus be deprived of its external blood-supply. As a consequence of this complication considerable portions of the bone may die, and in rare instances the whole diaphysis or shaft may be destroyed (Fig. 39). There then results what is called "total necrosis" of the bone. Usually, however, only a small part of the shaft suffers, and the sequestra thus formed rarely exceeds one-third or one-quarter the length of this portion of

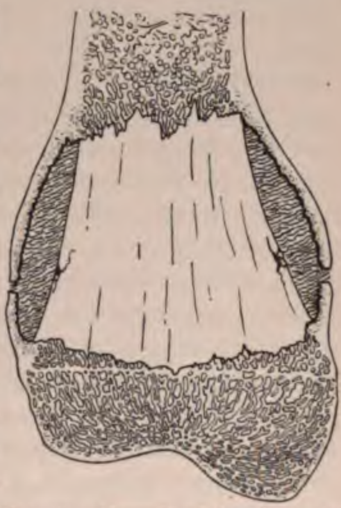

FIG. 39.—Necrosis of the Shaft and Periosteal Formation of Bone.

the bone. The extent of the necrosis is greater near the point of origin of the suppuration; that is, near the epiphyseal line, and at this point it may occupy the whole thickness of the bone. Nearer the middle of the shaft the necrosis is usually more superficial. It does not always follow that after the periosteum has been separated the portion of the bone thus exposed must necessarily die. Some of the periosteum thus separated may subsequently become reunited to the bone. The dead bone can usually be recognized, when inspected through freshly-opened abscesses, by its yellowish color and by the absence of the mottled appearance of normal bone. As the result of an extensive necrosis there may be, in rare cases, a *spontaneous fracture* of the bone at some point in its shaft. But this occurrence is usually prevented by the formation of new bone, which begins a few weeks after the old bone has been destroyed. Separation of the epiphysis also often occurs, but in the majority of cases the suppuration has only been sufficient to separate part of the epiphysis from the shaft of the bone.

When the bone dies it becomes a foreign body, still attached to the adjacent live bone, but separated from its covering of periosteum by a layer of pus. It lies, in fact, in the centre of an abscess. After the abscess breaks the periosteum comes more or less closely in contact with the shaft of the bone, and in a few weeks it is found that bony tissue is forming in the granulation layer lining the periosteal wall of the cavity. The formation of new bone takes place slowly, however, and it may be several months before sufficient bony tissue is found to supplant that which is gradually separating as a sequestrum. It is an important provision of Nature which does not permit the live bone to free itself entirely of the sequestrum until the work of the periosteum has been accomplished. Consequently, it is found that when the dead bone is fully separated and is ready to come away from the cavity in which it lies, it has become imprisoned in a wall of new bone (Fig. 40). The pus in which the sequestrum is bathed escapes through one or more fistulous openings in the newly-formed bone. In cases in which the periosteum has partly been destroyed by the septic process there will be no bony formation at that point, and the dead bone will then remain covered only by the soft parts, and can easily be reached and removed by the bone-forceps, or it may be forced out gradually from its bed by the exuberant granulations, or, if small in size, it may be expelled through a fistulous opening in the integument; in rare instances large fragments of bone may be extruded in this way. The pus exerts only a slightly solvent action upon the necrosed bone, but there are nevertheless frequently separated from the larger sequestra bony spiculæ, which from time to time are found in the discharges upon the dressings. The sequestrum is more likely to be affected by the young growing granula-

FIG. 40.—Separation of Sequestrum and Formation of Involucrum.

FIG. 41.—Unhealed Abscess-cavity, with Eburnation of the Surrounding Bony Tissue.

tion tissue, by which small sequestra may entirely be absorbed. The large portions of dead bone may, however, remain for years imprisoned in their bony cavities. After all sequestra have been discharged a suppurating cavity frequently remains with no tendency to heal, owing to the rigidity of its walls (Fig. 41). Such cavities may eventually become tuberculous. The epiphyseal cartilage in a certain number of cases remains intact; in other cases it is partially affected, and in still other cases it has disappeared, and under these circumstances it is usually found that the epiphysis or even the joint has been involved. Occasionally, as a result of the disorganization of the cartilage, there is a complete separation of the epiphysis from the diaphysis.

The *regeneration of the medulla* takes place from the perivascular connective tissue in the Haversian canals which open into the medullary cavity, and also from those portions of the marrow that still remain at the epiphyseal ends of the bone. From these points is developed a gray connective tissue which eventually assumes all the characteristics of the old medulla. On the borders of the newly-forming bone are found the osteoblasts from which the new bony tissue is developed. This new tissue is more porous and irregular in its arrangement than the old bone, and the bone-corpuscles it contains appear to be larger than those seen in normal bone-tissue.

In some places an absorption of bone may occur as a result of the inflammation. Here are found in the porosities of the bony tissue the large giant-cells or osteoclasts through which absorption takes place.

Occasionally there is found a *bipolar ostitis*, both juxta-epiphyseal regions of the bone being affected simultaneously. The disease begins in these cases at one end of the bone, and the infective material is conveyed through the medullary canal to the other end. At times the route taken can be followed throughout the canal; at other times the infection leaves no sign of its passage. In some cases these bone-inflammations may be multiple, several bones being thus simultaneously affected, such cases closely resembling pyæmia. The latter disease is not infrequently a sequel of the severer types of this form of bone-inflammation. Makin and Abbot report forty-one cases of bone-inflammation terminating fatally with symptoms of pyæmia. But many of the so-called cases of pyæmia originating from osteomyelitis are to be regarded as *multiple osteomyelitis*, the pyogenic cocci in such instances confining themselves to the osseous system. Such forms of osteomyelitis run a far more favorable course than pyæmia. In combination with such types there may be ulcerative endocarditis. Such a case has recently occurred in the hospital ward. A boy, twelve years of age, suffering from osteomyelitis of the shaft of the left tibia and the clavicle, had also marked valvular disease. The clavicle was treated by the removal of a large sequestrum involving the entire shaft of the bone, and amputation through the lower third of thigh was performed, as repeated operations by different surgeons failed to arrest the suppurative process in the tibia.

True *pyæmia*, however, may follow the outbreak of a violent type of osteomyelitis, and in certain cases the patient may die in a few days after the development of inflammation from *septicæmia*. The latter complication sometimes follows the opening of a bone-abscess. Such a case recently came under the writer's observation. The patient, a gentleman of about sixty years of age, had many years before suffered from osteomyelitis of the right femur, which had healed without necrosis of any extent. The abscess had been forming for about fourteen days, and when opened a large amount of fetid pus and sloughs was discharged, and the patient rapidly succumbed to acute septicæmia, which supervened. This case illustrates also the tendency to recurrence, which, after years of apparent health, the disease sometimes shows. These recurrent forms are said to be due to spores which have become encapsuled, and, owing to some local disturbance, have become free again.

Osteomyelitis is not always found in the long bones. It may have its seat in both the *short* and the *flat bones*. It is, however, much more rare in the latter situation, and many of these cases are mistaken for tuberculosis. In fifty-one cases reported by Fröhner the clavicle was found diseased eleven times, the scapula nine times, the ileum nine times, and the os calcis seven times. The disease may occasionally be situated in the so-called "joint region," and it then constitutes what is called *epiphyseal osteomyelitis*. There is in this form of the disease a primary localization of the inflammation in the articular extremity of the bone; that is, between the epiphyseal and articular cartilages. Under these circumstances the joint is involved at an early stage, for the more vascular epiphyseal cartilage offers a barrier to the spread of the disease toward the shaft of the bone, and the pus can therefore spread only in the direction of the articular cartilage. The joint affection soon overshadows the disease of the bone, and the patient presents the symptoms of a joint inflammation, the origin of which can only be brought out by a careful study of the case. Jordan, who reports two such examples, advises an early opening of the joint before it has been destroyed. Many such cases have undoubtedly been mistaken for tubercular disease.

We next come to a consideration of the *symptoms* of osteomyelitis. As the reader has already seen, this disease occurs most frequently in youth and after some slight injury or from exposure, or perhaps from no known cause. The patient suffers for several days from prostration, and complains of pain in some one joint or in the adjacent bone. Presently a severe chill occurs, which is followed by high fever, frequently of a typhoidal character. The pulse is weak and rapid and the face is flushed, the expression in the gravest cases being one of fright and stupefaction. The tongue is dry and coated, and there is frequently some delirium. The spleen is slightly enlarged, and there is often a foul diarrhœa. These are the symptoms of a grave septic infection of the system, probably from the ptomaïnes or toxines set free by the invasion of the bacteria. At first the only local symptom may be pain, but presently a swelling can be observed in the neighborhood of some joint, such as the knee, the shoulder, or the elbow, followed soon by more or less œdema of the adjacent soft parts, which œdema usually surrounds the affected limb. The swelling spreads in the direction of the axis of the bone, and the skin becomes œdematous and the veins enlarged. Although the skin may not yet have changed color, the part is excessively painful to pressure, the slightest movement of the limb causing the patient to cry out lustily. The pain is of a boring or almost breaking character, and at times throbbing; it is not necessarily always near the epiphyseal line, but may be near the middle of the shaft: it may exist for several days before the most careful examination can detect any local change or swelling. As the color of the skin changes to a reddish hue signs of fluctuation appear, and if the abscess is now opened the pus discharged is of varying character, according to the particular conditions of the case. At times the pus may be foul and filled with fragments of slough and decaying blood. Again, the pus may be found comparatively typical in character, and it will then be perceived that there are innumerable minute drops of fat floating in it. These fat-drops arise, as has been explained, from the decomposed medullary tissue, having forced their way out through the Haversian canals. Often, at this time, it will be found that the joint has begun to sympathize, and there may simply be catarrhal synovitis due to the neighborhood of the severe inflammation, or the joint, from having become infected, has begun to suppurate. In rare cases the disease in a bone can thus infect both articular cavities with which it is in contact.

The lungs are often also the seat of inflammations at this period, which inflammations may be caused by fat-embolism, such as is often observed after extensive fractures. This complication is seen in the early stages of the disease, and appears as a diffuse catarrh with abundant expectoration or with symptoms of œdema of the lung. Later pneumonia may be found developing, caused by emboli which have been detached from infected thrombi formed in the rich venous network in the medullary tissue. Metastatic deposits may also be found occasionally in other organs, such as the kidneys, and the symptoms of a genuine embolic pyæmia may, in rare instances, gradually develop. In the majority of cases, however, the situation is not so grave, and with the discharge of pus from the abscess the fever subsides and the case assumes a chronic type. It may then be found that the heart has been involved, and that there has been developed an endocarditis due to the attachment of the bacteria to the endocardium.

Returning, now, to the abscess which has just been opened, it will be found, on introducing the finger into the wound, that the bone has been denuded of its periosteum. If the pus has burrowed beneath the periosteum, the bone will be exposed for a considerable distance, and the surgeon will be somewhat startled to feel his finger gliding over the smooth and slippery surface of the shaft of the bone, which may be completely separated from the soft parts surrounding it. At other times an incision down to the bone may not liberate pus, and it then becomes necessary to open the interior of the bone before the seat of the suppuration can be discovered. With the discharge of pus the severity of the constitutional disturbance abates. As the suppuration gradually diminishes in quantity the fever disappears, leaving the patient greatly emaciated and with one or more sinuses leading to the diseased or dead bone.

As has already been seen, more than one bone may be affected at the same time, and this appears to be due not necessarily to metastasis, but to the simultaneous affection of one or more localities; at all events, these cases of multiple osteomyelitis must not be classified with those which succumb to genuine embolic pyæmia. The clinical picture in the two types is a very different one. The various points of inflammation develop synchronously or nearly so, and the virus does not appear to follow the laws of dissemination that hold in pyæmia. Many of these foci of inflammation may not come to suppuration. A tender lump may form at the end of a bone, and may subsequently disappear by resolution. At some of these points there appears to be a new formation of bony tissue instead of suppuration, and cases have been reported in which an increased length of the bone has resulted from inflammatory hyperæmia.

In not a few cases—particularly in infants and in young children—*acute suppurative arthritis* may occur as a result of the extension of the disease through the tender tissue of the epiphyseal cartilage. This form of osteomyelitis is frequently secondary to some of the exanthemata or to diphtheria or to pneumonia, and may be observed in many of the children frequenting the out-patient department of a large hospital. The amount of bone-destruction may in such cases be small, and the bone and joint may be restored to the normal state. This is the class of cases referred to by Koplik and Van Arsdale as being caused by the streptococcus infection. These authors recognize two forms of streptococcus osteomyelitis. In the *mild* form the disease is non-articular, the constitutional disturbance is slight, and it corresponds to Volkmann's catarrhal inflammation of the joint. The local inflammation is an acute one, and the joint suppurates, but the disease yields readily to surgical interference, and the function of the joint is gradually re-established. The *grave* type of the disease is insidious in its onset, the first thing noticed by the mother being the constitutional disturbance. "The child, if brought to the physician's attention, at once awakens solicitude. It lies quietly, pale, with sunken eyes surrounded by dark rims; its tongue is coated, fuliginous; its skin is dry, its temperature not being very high, however." Occasionally there are symptoms of pain, indicated by sharp little cries, and when certain parts are touched the suffering of the child is very great. In later stages the swelling of the joints is more pronounced. Several joints are usually affected, and aspiration reveals pus. Many of these cases belong to the class which has incorrectly been classified with pyæmia. Closer examination shows that the suppuration has emanated from the shafts of the bones, and that this portion of the bone may at times become extensively involved in the disease.

The *diagnosis* of acute osteomyelitis may, under certain circumstances, be attended with unusual difficulties. Most frequently the disease is mistaken for acute articular rheumatism. If a child is attacked in one or more joints simultaneously with symptoms of acute inflammation, and, later, symptoms of cardiac complication are developed, it is not surprising that the treatment selected should frequently be the administration of salicylic acid. Occasionally a patient is brought into the hospital in a more or less comatose condition, and it is only with great difficulty that there can be obtained from his friends anything approaching a history of the case. If under these circumstances there is as yet little local swelling around the focus of inflammation, it is not improbable that the diagnosis of typhoid fever might be made.

The disease does not always confine itself to the long bones, for not infrequently it is found that the carpus and tarsus, and sometimes the flat bones, like those of the cranium, are affected. Such cases might be mistaken for tuberculosis.

Tuberculous inflammations, however, are of a chronic type, while pyogenic inflammations are always acute. In doubtful cases the local conditions must carefully be studied, particularly with reference to their history. It will then be found that the pain is first noticed near the joint, and that pressure will bring out the fact that an acutely sensitive spot exists near the epiphyseal line. It is undoubtedly the fact at the present time that the true nature of these cases is not generally understood. Attention has not yet been drawn toward this subject, particularly to the importance of an early diagnosis, which may result in saving from destruction not only the bony tissue, but also a joint. The danger both to life and to the welfare of a limb is so great that it is to be hoped that those who see these cases in the early stage will realize the importance of a correct diagnosis and the necessity for prompt treatment. Much harm has been done by a former generation of surgeons, who taught that these cases were the result of periostitis—a diagnosis which inevitably leads to incorrect views as to the proper treatment.

The most frequent *sequel* of this disease is necrosis, which may be recognized by the presence of a fistulous opening leading to the dead bone. A probe introduced will readily detect the hard, smooth, bony substance lying at the bottom of the sinus. Occasionally the sinus is simply filled with flabby granulations, and it is probable that portions of the dead bone have been expelled by the pressure of the granulation tissue that has developed, or that the sequestra, if small, have been absorbed. The amount of bone disposed of by the process of absorption is in most cases exceedingly small, and large sequestra often remain for years unaltered (Fig. 42).

FIG. 42.—Necrosis of Femur, the result of Acute Osteomyelitis.

Spontaneous fracture is exceedingly rare. The writer remembers having seen but two examples. Separation of the epiphysis occurs, according to Ullmann, not as the result of the disintegration of the epiphyseal cartilage, but in consequence of a suppuration through the lower portion of the shaft, and it appears to occur quite independently of necrosis.

In some cases the inflammatory symptoms subside without the discharge of pus, and the patient appears to have recovered from the attack. Pain, however, recurs from time to time, and the patient may suffer for years from attacks of neuralgic pain, arising chiefly at night. There may be little if any enlargement of the bone to indicate the seat of the inflammatory process. Finally, an operation discloses an abscess situated usually near the epiphyseal end of the bone. The cavity formed in the bone has usually a smooth surface and contains true pus. The surrounding bony tissue is much denser than in the normal condition, and frequently presents the condition known as *eburnation* (Pl. I.). These abscesses are usually small, and they contain a drachm or two of pus, but occasionally they may attain great size. Stanley describes such a bone-abscess, the opening into which was closed by a cork that the patient was in the habit of wearing to protect himself from the discharge of pus.

Dislocation may occur as the result of several conditions. The joint may have become disorganized by the extension of the inflammation, the capsule and ligaments being then relaxed or partially destroyed. Roser has explained some forms of dislocation by an unusual growth of the ligaments due to hyperæmia near the necrosed bone. In some cases the growth of the bone is arrested by the destruction of the epiphyseal cartilage. If there is an adjoining bone which continues to grow, a displacement of the head of the adjacent bone may result. Nélaton mentions such a displacement of the head of the fibula in consequence of an arrest of development of the tibia.

In rare instances the granulations which protrude from the fistulous openings may begin to assume an active growth and the skin around becomes more or less infiltrated. The discharge is then more purulent in character, and it has an offensive odor. A new growth, which proves to be carcinoma, is taking place in the granulation tissue. Volkmann has collected thirty-two examples of this complication. Prompt amputation of the affected limb is of course the only remedy, as an early involvement of the inguinal glands may take place.

The *prognosis* of the disease varies, as may easily be judged, from the severity and the extent of the inflammation. The grave types of osteomyelitis that terminate fatally in a few days are happily rare. This form is perhaps most frequently seen in young children or in infants, and it is usually due to a streptococcus inflammation.

In a large majority of the cases the severe constitutional disturbance may subside in due time, and the chronic stage of the disease may be prolonged indefinitely. Nature does not appear equal to the task of removing the dead bone from its newly-formed cavity. The spontaneous removal of all sequestra is the exception. Even an empty cavity may be unable to heal, owing to the inability of its bony walls to shrink, and a "bone-fistula" may remain as a

PLATE I.

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Shaft of the Femur, showing the results of osteomyelitis. Thickening of bone with eburnation. The sequestra have long since been discharged.

permanent condition (Pl. I.). In some cases when the necrosis has been extensive, and when the suppuration has been prolonged and excessive, the patient may become greatly emaciated, and eventually amyloid degeneration of the internal organs may supervene, which condition is soon followed by a fatal termination of the case.

Since the pathology of osteomyelitis has been recognized and the point of origin of the inflammatory process has been definitely determined, the question of *treatment* has been much simplified. This is a disease which is caused by pyogenic cocci, and which terminates with hardly a single exception in suppuration. It is true that a certain number of cases are reported where the symptoms have subsided and the inflammation has terminated in resolution instead of in suppuration. Such cases are probably not true cases of acute osteomyelitis.

Counter-irritation, which was a mode of treatment much in vogue in former times, may be discarded. It is known that the actual cautery may in experimental cases of inoculation with pus-cocci prevent suppuration by stimulating the absorption of these organisms before they have had time to multiply, but such an agent would hardly act upon the deeply-seated foci, the presence of which in bone is not detected until the disease has made too much progress to be checked. In the early stages, before a diagnosis has been made, much may be done to mitigate the sufferings of the patient. The limb may be immobilized by a splint and pain be relieved by the application of ice-bags or of poultices. The treatment of this disease from the earliest moment that a diagnosis can be made is eminently a surgical one. As in cases of suppuration in the abdominal cavity, pus must be removed before it has an opportunity to effect serious or fatal injury. Although in appendicitis some surgeons still hesitate to operate, as many cases recover without suppuration, in osteomyelitis pus is always formed, and must be removed—the sooner the better.

The problem differs somewhat according to the stage the disease has reached when the patient first comes under observation. In the earliest period the pus is still confined to the interior of the bone, and a well-formed abscess may not yet have developed. It is uncertain whether the virus may not infiltrate the whole medulla and destroy the entire shaft or endanger the life of the patient. In these cases an opening should not only be made to allow the pus to escape externally, but an attempt should also be made to remove the infected area itself, and thus to arrest the inflammation. Some writers advise an attempt to remove the pus by boring with a drill numerous small holes through the soft parts and the bone. This is Ullmann's method, who makes the punctures from 2 to 3 centimetres apart. Kocher not only punctures the bone, but also injects carbolic acid with a view to disinfecting the foci of suppuration. Such procedures seem hardly suited to ordinary cases of bone-suppuration, but might be used on some of the smaller bones, such as the alveolar processes of the jaw, where the amount of pus is exceedingly small. In typical cases of this disease a prompt incision should be made through the soft parts to the bone, which must then be opened with the gouge or with the trephine. Frequently no signs of inflammation will be detected until the medulla has been reached; then a few drops of pus, collected in small foci, may be revealed, or the discharge may merely be of a sero-purulent character, or the medullary tissue may be gangrenous. The infected portions of the medulla must carefully be scraped away, and if this operation is thoroughly performed the wound may be left in a completely aseptic condition. The wound should not be closed, but, after having been thoroughly washed out with some disinfectant, should be stuffed with iodoform gauze. The result of this treatment is subsidence of the febrile symptoms and great relief of the pain. If, however, the high temperature recurs and the bone again becomes painful, it may be necessary to enlarge the bony opening and to scrape away any portion of the medulla found to have become infected. A stout, sharp curette is the most useful instrument for this purpose: it should be made in various sizes, so as to reach all corners of an infected area. The Esmarch bandage should always be applied before operating upon the bones of the extremity, the surgeon being thus enabled to carry out with great precision all the details of the operation and to see with great ease all the pathological changes.

When the pus has reached the surface the periosteum is dissected from the bone for a certain distance and the soft parts are invaded. This condition is readily recognized by the swelling and the redness of the surrounding integuments. In such cases the external abscess must be laid open and disinfected by curetting and by washing its walls; the periosteum must be opened freely, and a search must also be made for the point of origin of the inflammation in the bone. This is a precaution which surgeons often neglect, thinking that the case is one of "suppurative periostitis," and that it is unnecessary to search farther. The teachings of pathology must be remembered here, and search for pus must be made near the epiphyseal line. No operation which does not include an opening into the bone should be regarded as a completed one. French surgeons have long recognized the importance of this detail. Lannelongue advises that the trephine should be placed near the epiphysis, and that a second opening should be made into the shaft of the bone to open the medullary canal, which in young subjects does not always reach to the epiphyseal line. If the periosteum has peeled off for a great distance, it may be necessary to make a third opening. Trephining, he thinks, should also be employed in osteomyelitis of the flat bones, such as the cranium. Multiple openings are only advisable in very extensive disease of the medulla. Under ordinary circumstances an opening near the epiphyseal line should be made, and be sufficiently enlarged with the chisel or the gouge to expose the diseased area.

Formerly it was advised not to open these abscesses until the last moment, when the surrounding inflammation had had time to protect the tissues from the decomposing medulla. It was found that in many cases of early opening the patient succumbed to septic infection, but this rule does not hold good at the present time. The custom serves, however, to emphasize the importance of thoroughly opening and disinfecting these treacherous abscesses.

So serious were the results following these operations before the days of antiseptic surgery that amputation was freely advised as the only means of saving life. The fine specimens of bones containing sequestra in many of our museums are silent testimony to the popularity of the discarded treatment. Chassaignac laid down careful rules for amputation in this class of cases, and Roux held that disarticulation was the only proper remedy, as amputation through the continuity of a bone did not avail to prevent the spread of the inflammation. Amputation is now resorted to only in exceptional cases, when all other means fail to arrest the suppuration or the case approaches a fatal issue. When such abscesses have been opened and disinfected drainage-tubes should be introduced down to the medulla, and the abscess-walls should be packed with iodoform gauze. The whole limb is then swathed in a voluminous antiseptic dressing and is placed upon a splint. If all goes well, this dressing need not be changed for several days. But if constitutional disturbance continues, the dressing should be removed and the wound be thoroughly washed out with a disinfectant. A moist antiseptic dressing may in such cases be substituted for the dry dressing. A large cotton poultice soaked in a solution of sulpho-naphthol (1 : 250) may be applied and changed once or twice a day.

In those cases where the joints are involved—which complications occur chiefly in infants and in young children—the following rules, laid down by Van Arsdale, should be observed: As soon as the joint appears swollen and becomes painful, it should be aspirated under the strictest antiseptic precautions, and if pus is found the joint should be laid open, drained, and dressed antiseptically. Usually one incision will be sufficient for this purpose, but in some instances counter-openings with packing of the joint, or even resection of the joint, may be necessary. Resection of the hip is more frequently performed than that of the other joints. Volkmann found the prognosis more favorable in resection of the hip for this disease than for tuberculosis. Special attention should also be given to the shaft of the bone in these cases, and incisions should be made for the purpose of exploring this portion of the bone. If it is necessary to remove portions of the shaft, Van Arsdale dwells upon the importance of working upon the two regions separately, with the view of sparing, as much as possible, the epiphyseal line, and thus giving an opportunity for the future development of the bone.

Many cases of osteomyelitis resist all efforts to arrest the inflammation. Suppuration continues, and the shaft of the bone may become more or less disorganized. In other cases the pus may burrow so freely under the periosteum as to denude the entire shaft. Under these circumstances the question has been raised as to the justifiability of a resection of a considerable portion of the shaft of the bone. Ollier recommends this operation only as a last resort. It should be performed as late as possible, as the periosteum may then have reached the reproductive stage. The objection to this operation is the uncertainty of the reproduction of the bone; a large number of operations are reported where only a partial renewal of the diaphysis has taken place. Marchant reports a case of resection of the shaft of the tibia in a child sixteen years of age. This patient, when seen five years later, walked on the side of the foot. A case of resection of two-thirds of the inferior portion of the radius was followed by forced extension of the hand backward and outward. Marchant reports successful cases of resection of the shaft of the humerus and of the femur, and successful cases are also reported by Holmes, Cheever, and many other surgeons. Petersen reports the case of a sailor, seventeen years of age, who had been suffering for eight days from osteomyelitis of the clavicle. The entire diaphysis was dissected by pus and was removed. The bone was renewed in four weeks, and the wound was healed six weeks after the operation. In the bones of the extremities such a condition would be, according to Ollier, extremely unfavorable for the repair of bone, and if the periosteum is dissected off in this way by pus, its osteogenetic elements will be destroyed. The cases favorable for resection are those in which the periosteum is thick and covered with osseous plates, and this condition is found in the later stages of the disease. Certain portions of the skeleton are more readily reproduced than others; as, for instance, the lower jaw and the lower portions of the tibia. The prognosis of resection is most favorable in children; after the twentieth year resections of the shaft are problematical. In many cases in which the operation has been attempted the amount of shortening of the limb has been excessive. In resections of the shaft of the bone care should be taken not to interfere with the epiphyseal cartilage. The incision through the periosteum should carefully be made, and this membrane should be bruised as little as possible during its separation from the bone. The edges of the periosteum should subsequently be sutured with catgut, and a small drain of gauze should be left in one or in both ends of the incision. The limb may then be immobilized on a splint during the subsequent treatment. By far the greater number of cases of this disease come under the notice of the surgeon during the stage of necrosis; that is, after all acute symptoms subside and a fistulous opening remains to mark the site of the abscess.

It is generally agreed that sufficient time must be allowed to elapse for the sequestrum to separate from the live bone before the attempt is made to remove it. It is quite difficult to determine where the line of demarcation is to form, and it often happens that a piece of bare bone of considerable size is gradually covered over by granulations and the wound heals without any loss of bone. The bone receives its nourishment from the vascular medulla, as well as from the periosteum, and the separation of the latter does not therefore necessarily result in death of the bone. An early interference may therefore not only involve the removal of a needlessly large quantity of bone, but may also disturb the vitality of the surrounding bony tissue and cause the separation of new portions of the bone.

The time required for the separation of a sequestrum varies greatly. At the epiphyseal line the bone may separate in a few weeks, but in the shaft of the long bones it may be several months before the sequestrum is fairly loosened. A fragment of cortical bone usually separates much more rapidly than some of the deep-seated, spongy sequestra. There is less danger of spontaneous fracture if the sequestrum is allowed to remain until the involucrum has developed and sufficient new bone has thus been formed to replace the old.

Usually, when a typical case of necrosis presents itself for treatment, the sequestrum is found deeply seated within a cavity formed by new bone, which has grown exuberantly and lines for some distance the walls of the sinus leading to the dead bone. When a considerable quantity of periosteum has been destroyed by the suppurative process, the dead bone will be found uncovered by new bone, and may, consequently, much more easily be reached. The cicatricial tissue about it, however, is dense and unyielding, and in any case, therefore, free incisions are necessary to lay bare the foreign substance which is to be removed. One should always be prepared, therefore, for a long and tedious operation and for extensive dissection in these cases; for it is not only necessary to remove the dead bone, but the cavity must be so treated as to heal permanently. The rigid walls of an old involucrum cannot shrink together, and they are covered with feeble granulations which may contain a miscellaneous assortment of bacteria. These are the conditions which favor the persistence of a "bone-fistula." The old method of treatment, which consisted principally in fishing for fragments of dead bone with the forceps, cannot too strongly be condemned. Modern surgery demands a completed operation; that is, one which ensures rapid and permanent healing of the wound.

The limb having been thoroughly cleaned and the sinus having been syringed out with some mild antiseptic for several days before the operation, an antiseptic dressing should be applied, so as to diminish as much as possible the septic condition of the parts surrounding the wound. The Esmarch bandage having been so adjusted as to render the limb bloodless, the sinus should be laid open to its point of entrance into the bone. In some cases it will be found impossible to do this, owing to the tortuous nature of the canal and to the presence of a large vessel or a joint-cavity in the immediate neighborhood. In necrosis of the lower portion of the diaphysis of the femur the sinus often opens through an intermuscular space near the route of the femoral vessels, and the surgeon must proceed cautiously to avoid wounding these vessels. It may be more convenient under these circumstances to approach the bone-cavity from the opposite side of the thigh if it be necessary to chisel away a large surface of new bone. A clean and straight incision should be made through the soft parts and the periosteum, and the surface of the bone should be exposed freely. The entire roof of the suppurating cavity should then be removed with the trephine or the chisel or with both. This operation is necessary not only to ensure complete removal of the sequestrum, but also to expose the lining pyogenic membrane, so that it may be scraped away thoroughly and nothing but healthy tissue be left behind. The same scrupulous care should be given to this part of the operation that the dentist employs in treating a carious cavity in a tooth. The wound, as now shaped, is no longer a fistulous tract, but a trough-shaped affair with a large opening. It may now be treated so as to heal by granulation or to unite by first intention. In the former case the wound, after being thoroughly irrigated with a weak solution of corrosive sublimate to wash out all particles of bone or of tissue, is stuffed with iodoform gauze, which is used in sufficient quantity to keep the upper portions of the lips of the wound well separated from one another, so as to allow the wound to heal slowly from the bottom to the surface without resuming a fistulous shape. This method consumes a considerable period of time, and may, owing to neglect on the part of the patient, terminate in a fistula which may require months to heal.

Attempts have been made to hasten the healing process by plastic operations. Flaps of skin have been turned into the long gutter, so that the exposed surfaces of bone may be covered in by the yielding soft parts. Fragments of bone still adhering to the periosteum have been loosened from the sides of the trough, and have been pushed in so as to obliterate the cavity.

Schede proposed to fill up this deep cavity in the bone with blood-clot, which subsequently becomes "organized," after the manner originally described by Lister. The wound must be made absolutely aseptic by chiselling away all diseased or infected bone and cutting away edges of skin and tissue which have been saturated for a long time with the discharges. Any suspicious corners must be swabbed out with strong solutions of carbolic acid or of permanganate of potash, and the wound must be drenched and scrubbed freely with milder antiseptic washes. The edges of the periosteum and integuments are now approximated by sutures, which should be made of catgut and be applied as buried sutures. A small strip of protective or rubber cloth is placed over the wound, and before the tourniquet is removed an antiseptic dressing is firmly bound on, to prevent the escape of blood which oozes from the walls of the wound and fills the cavity. This dressing should not be disturbed for two weeks, at the end of which time, in successful cases, the wound will be found to have healed by first intention.

It is not always easy to retain sufficient blood in the cavity thus prepared to fill it completely, in which case the delicate clot gradually melts away as granulation tissue forms, and the wound has to be reopened and allowed to heal from the bottom. A partial success will, however, shorten considerably the healing process.

Senn conceived the idea of utilizing decalcified bone-chips as a "filling" for these bone-cavities. These bone-chips are preserved in an alcoholic solution of corrosive sublimate or in a solution of iodoform in ether. The most favorable cases for this method are bone-defects due to the removal of tumors, or bone-lesions other than those produced by pus-cocci. The next most favorable cases are primary circumscribed inflammations in the epiphyseal ends of long bones. This method is also applicable after operation for necrosis. After the cavity has been disinfected and dusted over lightly with iodoform the chips, previously washed in an antiseptic solution, are dried upon a gauze compress, and are then put into the cavity until it is packed with them as far as the periosteum. The periosteum is now sutured with absorbable buried antiseptic sutures. Buried sutures may also be used for the soft parts above. The skin is finally sutured with silk. An absorbable antiseptic drain of catgut is used at the extremity of the wound to allow the escape of the superabundant blood, which flows in as soon as the tourniquet is removed. The remaining blood coagulates and forms a matrix in which lie the bone-chips (Fig. 43).

FIG. 43.—Healing of Blood-clot, and Senn's Bone-chips.

A voluminous antiseptic dressing should be applied to the limb, which should be confined in a splint, and the dressing be allowed to remain undisturbed for two weeks. Rest should be enforced until the process of repair in the interior of the bone has been completed, embracing a period varying from four weeks to three months.

Many successful cases testify to the value of both the above methods. They cannot, however, be carried out in difficult cases except by the trained surgeon with every possible convenience at his command. Many bone-cavities communicate with the exterior surface by numerous tortuous channels, whose walls contain septic material which is sure to contaminate the blood-clot. These methods are better adapted to cavities not made by suppuration or to pus-cavities of limited size and readily accessible to the gouge or to the curette. In some of the more complicated cases of necrosis a preliminary operation might so far restore the neighborhood to a cleanly condition that the blood-clot method might later be adopted with success. When, however, the cavity has been opened and cleansed in the thorough manner already described, there is every reason to hope that a permanent healing of the wound may be completed by the process of granulation in from three to four months' time, and this is the method the writer would recommend in the majority of cases. The attending physician should never undertake the care of such a case if he contemplates only halfway measures. If not prepared to go through with the labor of a completed operation, it will be better for his reputation to have nothing to do with the case.

IX. THE PROCESS OF REPAIR.

FORMERLY the changes brought about in the tissues by means of which repair was effected were supposed to be caused by inflammation. It was thought that a smart inflammatory reaction was necessary to glue the lips of a wound firmly together. Aseptic surgery has demonstrated the error of this view, and it is now known that the two processes are quite independent of each other.

The action of the cells in repair is a question about which there has been a great deal of dispute. Some of the changes which they undergo during inflammation have already been considered. Suffice it to say here that Virchow adopted the view that the large number of new cells seen during the reparative process were formed by a proliferation of the pre-existing cells of the part. Cohnheim set aside this view, and replaced it by his theory of the action of the leucocytes, which were supposed to supply all the material for the new tissue that was formed. This theory held sway for nearly two decades, but a more perfect knowledge of the histology and the physiological action of cells has partially restored to the fixed cells of the tissues their former prominence in the process of repair. The old theory of cell-proliferation assumed that all cells underwent what is now understood as direct cell-division; that is, a segmentation of the nucleus having taken place, there was a division of the protoplasm by means of which two cells were formed.

The theory of *indirect cell-division*, or *karyokinesis*, has now supplanted that of *direct* cell-division, which is supposed to take place only in those cells having no power to form new tissue, such as the leucocytes, the rôle of which in repair is now regarded as quite subordinate. One of the earliest changes that is seen in the cells of a part when repair is going on is an increase in their size. At the same time peculiar changes are taking place in their nuclei. The nucleus consists, according to Ziegler, of a membrane and contents. The latter is composed of a network of nucleoli, granules, and threads which are somewhat opaque, and which can readily be stained by pigments. This network lies imbedded in a soft material which is incapable of receiving color. During the process of division the network of the nucleus undergoes a series of typical changes of form which give origin to the term *karyokinesis* (κάρυον, nucleus; κίνησις, movement) (Fig. 26). Flemming uses the term *karyomitosis* (μίτος, a thread), denoting the thread-like appearance of the network. That portion of the material of the nucleus which stains readily is called "chromatin."

The nucleus, in fact, is a highly organized substance by which the cell transmits its peculiarities to its descendants. The protoplasm of the cell is the medium of communication with the surrounding tissues, and it regulates the nutrition.

When the cell is about to undergo division there is a marked increase in the amount of chromatin of the nucleus; the threads of the network become much thicker, and they seem to be coiled loosely together; at the same time numerous nodules appear in the network (Fig. 26[1]). The nucleolus now disappears, and the membrane of the nucleus, losing its ability to take the staining fluid, is soon lost (Fig. 26[2]). The threads become gradually thicker, and arrange themselves in a series of loops which point toward the equator of the nucleus, and form, when seen from the poles, a stellate figure known as the *mother-star* (Fig. 26[3]).

The next change in the grouping of the threads is known as *metakinesis*, and consists in a movement by which these loops are gradually turned around so as to point toward the poles of the nucleus. As the loops which are now found in two separate groups gradually approach the poles, there are formed two stellate figures (one near each pole), which are known as *daughter-stars* (Fig. 26[4]). Their stellate appearance is well seen when viewed from the poles. These daughter-stars gradually resume the thread-like coils found in the original nucleus, and eventually form a network. At the same time a new membrane is formed around each coil (Fig. 26[5]), and two nuclei are thus developed (Ziegler). During nuclear division the protoplasm of the cell undergoes certain active rotary movements: as the result of these movements there is the formation of a bright zone around the nucleus and of radiating lines at the poles of the cell. Finally, there is a segmentation of the protoplasm of the cell, which segmentation begins about the time the daughter-coils are formed. Considerable variations may take place in nuclear division, but the above is the type of the process.

The division of the nucleus is usually bipolar, but it may be multipolar. In this way many nuclei may form. If the segmentation of the protoplasm is delayed or if it does not occur, the large many-nucleated cells known as *giant-cells* are developed.

The cells that multiply and take part in the formation of new tissue are the fixed cells of the connective tissue and the cells forming the walls of small blood-vessels, which cells also take an active part in this process. Under these circumstances the endothelial cell is seen much enlarged, projecting into the lumen of the vessel and undergoing mitosis. Some of the new cells come from a distance, and belong, therefore, to the variety of wandering cells. The leucocytes wandering into the part are frequently present in large numbers, particularly when there is much inflammation, but play no active part in the formation of new tissue.

While these new cells are collecting the old tissue has perhaps softened and broken down. The intercellular substance becomes more or less granular, and less is seen of it. In this way there is formed a new temporary tissue, known as *granulation* or *embryonic* tissue. The cells found here are the leucocytes, single-nucleated or polynucleated, and the cells which are actively forming new tissue are called "formative cells," "embryonal cells," or "plasma cells." They have a granular protoplasm and a bright, round, and large nucleus, which stains readily, giving the cell an appearance strongly suggestive of epithelium. They are therefore usually called "epithelioid cells." Owing to their power to form connective tissue they are also called "fibroblasts." They have various forms: some are spindle-shaped, others pear-shaped, and many may have several prolongations.

Ballance and Edwards describe the plasma-cells seen in small glass chambers placed beneath the skin of animals, according to Ziegler's method, as mostly plate-like cells extended into so thin a film that their exact limit was hard to determine. They were distinguished from leucocytes by their larger size and coarser granules and by the constant presence of a single clear nucleus of oval figure. In specimens from chambers that had rested seventy-two hours these cells showed vacuolation. In some of these vacuoles a leucocyte or red corpuscle could be found. The leucocytes near these cells appeared to serve as a pabulum for them. Not all the leucocytes were disposed of in this way: some of them were dissolved in the tissue-plasma exuded by the plasma-cells (a protolytic ferment).

Grawitz believes that many cells—his so-called "slumbering cells"—develop from fibres: nuclei first appear within fibres, and the cell-body is gradually formed around them. These cells are capable of division like fixed cells, and when cicatrization takes place they pass into their fibrous condition again and become slumbering cells once more; that is, they now no longer react to staining processes.

When connective tissue is formed, there is seen between these slumbering cells a more or less homogeneous intercellular substance in which fibrillæ later make their appearance. The fibrillæ, however, may form directly without the intervention of a homogeneous material. According to some observers, these fine fibres are formed by a splitting up of the protoplasm of the cell itself: other observers, however, assume that an intercellular substance is exuded, as it were, from these cells, and that in this medium the fibrils are subsequently formed. When the development of fibres has reached a certain point the formative cells or fibroblasts begin to diminish in number, those which are left being enclosed in narrow spaces between the bundles of new fibres.

According to Grawitz, as already seen, the new cells are developed from the so-called "slumbering cells," which lie, undetected by staining fluids, in the fibres under ordinary circumstances, but when in a state of irritation they become active once more and are capable of forming new tissue. This view, though endorsed by many, has not met with general acceptance.

Thus far, connective tissue only has been considered. The cells of this tissue, like all other cells, can of course solely produce those of their own blastodermic layer. An epithelial cell cannot produce cartilage or bone. Some cells have permanently lost their power to proliferate, such as the epidermal cells and the non-nucleated blood-corpuscles; also, probably, the ganglion-cells. Epithelial cells, gland-cells, connective-tissue cells, periosteal and bone-marrow cells, possess very active reparative properties.

Attention will now be given to the *healing of a wound* through the skin and subcutaneous tissue. When there is made an incision which freely divides these structures, their natural elasticity separates the edges of the wound from one another, and the wound is said to "gape." When only smaller vessels are cut, the bleeding either stops spontaneously after exposure to the air or it may readily be controlled by the temporary application of pressure-forceps. When the larger vessels have been tied and the bleeding ceases, the edges of the wound are brought together by suture. If the wound is deep, it may be necessary to pass some of the sutures to an unusual depth, or buried sutures may be applied to bring the subcutaneous fatty tissue or muscular fibres into their proper position, so that no "dead spaces" are left. In other words, the walls of the wound must be brought in contact throughout, otherwise the oozing of blood and serum that almost invariably occurs during the first few hours may separate the walls from one another and thus delay the healing process.

If the wound has been preserved in an aseptic state, there are no symptoms of inflammation seen during the healing process. The parts appear during the next few days almost exactly as they were at the time the wound was first dressed. There is usually a certain amount of swelling and tenderness in the part. The former symptom is due to the exudation of serum, which collects in the interstices of the tissue or between the lips of the wound. In large wounds the amount of serum thus exuded may be considerable. It is estimated that the quantity of serum which flows from the wound of an amputated hip-joint may exceed a pint in the first twenty-four hours. There is also an increased number of cells in the part, and a deposit of fibrin both in the lips of the wound and in the interstices of the tissue. In consequence of this exudation the parts immediately about the wound are somewhat firmer to the touch than they were before.

Firm pressure and careful adjustment of the edges of the wound will generally greatly diminish the amount of the exudation. The dressing, however, is usually soaked with a sero-sanguinolent discharge during the first twenty-four hours. On this account some surgeons still prefer to place a drain of some kind between the edges of the wound for twenty-four or forty-eight hours, even though they are quite confident of its aseptic character. The primary oozing of serum is thus disposed of, and undue pressure on sensitive or on vital parts, such as the brain, is avoided. A small strand of sterilized gauze or a thoroughly sterilized drainage-tube is sufficient for the purpose. If the drain is not removed before the end of the second day, it is liable to cause suppuration. Even though the dressing be perfectly aseptic, the staphylococcus epidermidis albus (existing in the deeper layers of the epidermis) may thus find its way into the interior of the wound.

If the stitches are removed on the fifth day in wounds where there is no tension, the skin will remain adherent, although the union is still far from firm. The edges of the wound are, in fact, only glued together during the first two or three days by the coagulated fibrin.

In large wounds coaptation of the parts on the surface is rarely so perfect that complete union of the edges of the skin takes place from one end of the wound to the other. At one point the skin may be at a slightly lower level than at another point, or the skin may be curled in by the stitches. Small fragments of skin may have been bruised or unduly constricted, and minute sloughs may form in this way. Consequently, after the dressing has been

PLATE II.

Healing by First Intention of an Abdominal Wound (sixth day): above is seen a suture infiltrated with leucocytes; below are seen the edges of a divided linea alba separated by a blood-clot; upper border, skin; lower border, peritoneum. Cell-infiltration is seen only along the line of incision.

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removed minute scabs are found here and there along the line of the incision that do not drop off for several days. The points of exit of the suture are also marked by small crusts. During this period the wound is in a very receptive state, and any undue strain or neglect may favor the development of a minute focus of suppuration under some one of these scabs, which may result in an abscess. The soft new tissue has feeble power of resistance to the invasion of the bacteria. A large wound cannot be said to have passed through its period of danger before the end of three weeks. This mode of union is termed *healing by first intention* (Pl. II.).

If the wound has not been kept aseptic, symptoms of inflammation appear on the second day. The edges of the wound are somewhat reddened, and much more tender than in the aseptic wound. By the third day a slight amount of pus may emerge from some portion of the superficial structures or from a stitch-hole. A moderate amount of sepsis will not interfere with a prompt healing of the wound, and if a moist antiseptic dressing is applied to favor the escape of the small quantities of pus found here and there, the wound may practically heal by first intention. In such wounds, however, it is probable that there will be left a small sinus which may not heal until the end of two or three weeks.

If sections of the wound, made at different stages of the healing process, are now examined, the following appearances will be observed: At the upper margin of a wound two or three days old the epidermis is usually found more or less curled in. Wherever in the deeper layers of tissue the fibres have retracted, there are found small clots of blood, which serve the useful purpose of filling out all irregularities. If the section has been stained carefully, all cell-structures stand out with great distinctness, and the line of the incision is indicated, even with a very low power, by a row of cells which have accumulated at the edges of the wound on either side.

In cases running an aseptic course the number of cells is comparatively small, and they are not seen except in the immediate vicinity of the wound (Pl. II.). There is an accumulation of cells around some of the blood-vessels, and rows of small round cells may be seen extending between the bundles of fibres toward the margins of the wound. The small clots found in clefts between retracted fibres are invaded with numerous leucocytes. The number of vessels does not appear to be increased, and it is probable that in many instances the formation of numerous vascular loops, so often described, does not take place.

In healing by first intention there is at first no reddening of the cicatrix, which, however, becomes red and prominent at the end of a few weeks, and it is probable that at this period new vessels have formed. In many parts of the body the scars are almost imperceptible from the beginning, and in these cases there is little if any increased vascularity. According to Thiersch, the plasma-canals communicating directly with adjacent vessels contain blood, by which the tissues are provided with nutriment until new blood-vessels are formed. When there is considerable amount of inflammation complicating the healing process, there is a formation of new vessels, which develop in the shape of loops projecting toward the edges of the wound. Experimentally it has been shown that in animals these vascular loops may unite across the lips of the wound in about ten days.

A careful inspection of several sections usually discloses the fact that minute fragments of the edge of the wound or of the deeper structures have become necrosed and are in process of absorption. The leucocytes are markedly increased in numbers around such masses, and also around fragments of the ligature, between the fibres of which many cells make their way. It is evident that the leucocytes are endeavoring to break up and absorb all material that is in the nature of a foreign body (Pl. II.).

If a wound is examined near the end of the first week, it will be found that the round cells are beginning to disappear, and in their place will be seen spindle-cells or fibroblasts. These are the cells which have developed from the pre-existing cells of the part. The surrounding cells or leucocytes take no prominent part in the process of repair, but serve as nutriment for the forming tissue. Between the fusiform cells new intercellular substance is developed in the way already indicated, and thus new fibrous tissue is formed. As the fibres develop many of the fusiform cells undergo granular degeneration and are absorbed. The same fate also awaits such leucocytes as have not already found their way through the lymph-channels back into the circulation. In this way is formed cicatricial tissue, which differs from normal fibrous tissue in that the fibres do not run parallel with one another, but interlace in various directions, forming a felt-like mass which is very elastic and has great contractile power—a peculiarity which serves a useful purpose in drawing the edges of the wound firmly together. The scar when gradually formed becomes prominent and red, and is a source of disfigurement on an exposed surface. The contractile nature of the scar-tissue, however, gradually constricts, one after another, the delicate capillary loops that have developed, so that eventually there is less blood flowing through the part than there was before the injury. This change takes place slowly, and a year or more may elapse before the red scar has faded away and given place to a line that is somewhat paler than the surrounding healthy skin.

Healing by second intention occurs when the edges of the wound have not been brought together. In this case a considerable quantity of new tissue is formed, by means of which the cavity is built up from the bottom. If a wound is made (by the removal of a breast) so large that the skin cannot be brought together, it will be found, after the bleeding has been arrested, that in the portion which has not been closed the bottom is covered by the red muscular tissue of the pectoralis muscle, and that the sides are composed of the yellow adipose tissue. The anatomical structures are somewhat obscured by the formation of a thin coagulum of blood which fills out the irregularities of the surface on the bottom and around the edges of the wound. After the lapse of several hours a transparent film forms over the whole surface, covering it like a varnish. The wound is said to have "glazed." This appearance is produced by the exudation of serum from the blood-vessels and by the coagulation of the fibrin it contains. Formerly surgeons were in the habit of waiting for this stage of the healing process before closing the wound, as it was supposed that the opposing surfaces would then quickly adhere and would not be forced apart by the exudation of serum.

This film does not remain transparent a long time, for soon minute opaque spots begin to appear here and there, caused by the accumulation of leucocytes. The coagula of blood on the surface also soften, and the color runs through the transparent layer and stains it a dirty red. The normal tissues now begin to disappear, and the layer formed over them soon becomes further discolored by the liquefaction of minute sloughs of tissue which have been bruised by the knife. The surface of the wound no longer has its clean appearance, but it is covered with a dirty membrane having a mixture of ill-defined colors. This membrane remains for three days, at the end of which time it appears to have separated from the subjacent parts by the formation of a fluid beneath. The membrane finally floats off with a free flow of pus, and there is disclosed a layer of bright-red tissue studded with very minute elevations, known as *granulations*. The wound is said to have *cleaned off*. It will be noticed at this stage that the wound is much shallower than it was before. The tissue of which these granulations are composed is known as *granulation tissue*, and it is by the growth of this tissue that the cavity is filled. In a few days this layer reaches the level of the surrounding skin, and it is now seen that the area of the wound is smaller than it was at the beginning. The next stage in the healing process is the covering of the granulations with epidermis. If the margins of the granulating tissue be examined with a lens, the presence will be noted of a transparent film, through which the granulations may still be seen, although they have flattened out. As this transparent film works its way toward the centre of the wound the older layers change to a pearly-white color and become opaque. This process (Fig. 44)

FIG. 44.—Healing by Second Intention.

consists in the proliferation of epithelial cells, by which means the new granulation tissue is eventually covered over. These cells cannot form independently in the centre of the wound, although the new epithelial cells possess amœboid movements and may wander a short distance from the margin of the wound. The growth is not unlike the formation of ice on a pond, the water around the edges of which first becomes covered by a thin film of ice, which by a process of continuous formation finally covers the deeper waters at the centre.

In large wounds the surrounding epidermis is unable to supply a sufficient number of cells to cover the open surface; consequently, the wound would not heal were it not for the power of the cicatricial tissue forming beneath the granulations to contract and draw the edges of the wound toward one another. This contractile power is caused by the shrinkage due to the absorption of the soft cellular and vascular granulation tissue and its replacement by dense fibrous structures.

If the granulation tissue is studied under the microscope, there will be found a tissue crowded with small round cells and containing a large number of small blood-vessels, which tend to run in a vertical direction toward the surface of the wound. An examination of this tissue with a high power of the microscope shows that there are not only a large number of leucocytes, distinguished by their numerous nuclei which come out very characteristically when stained, but that there are also many single-nucleated leucocytes and larger epithelioid cells. Near the surface of the granulation tissue the leucocytes abound (Fig. 45). Lower down are

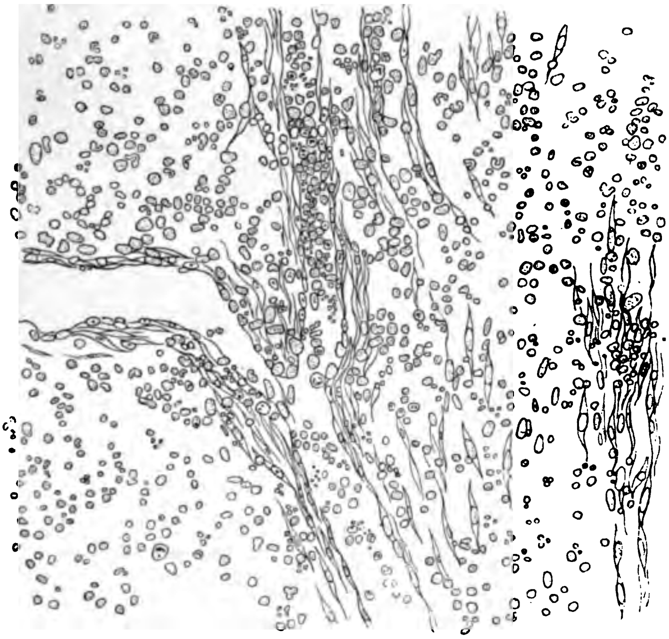

FIG. 45.—Vascular Spaces with Tissue filled with Leucocytes near the Surface of Granulations.

found the larger cells, particularly in the vicinity of the blood-vessels, from whose walls an active cell-growth appears to take place. Still lower, the cells assume a spindle shape, and the deepest layers of all consist of bundles of spindle-cells running in a horizontal direction beneath the surface. In wounds that have remained open for a long time or in ulcers this deepest layer has become quite fibrous, and it seems to serve the purpose of walling off the surrounding healthy tissues from the imperfectly-formed tissue above, which in many cases contains the elements of disease (Fig. 46).

Many observers describe a rich growth of blood-vessels, arranged in festoons and loops, running vertically toward the surface, and

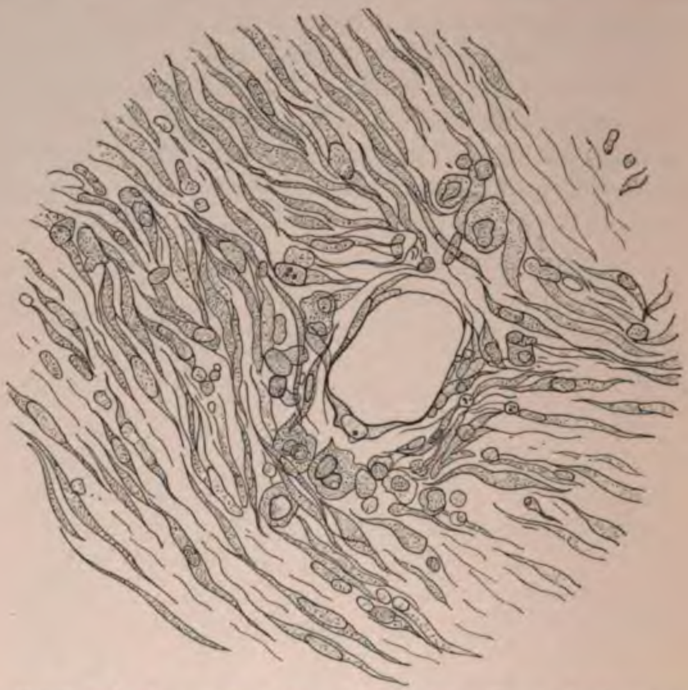

FIG. 46.—Detail Study from a Deep Layer of Granulation Tissue, showing a vessel with epithelioid cells and spindle-cell growth.

ascribe to the presence of these loops the little hillocks of cells so characteristic of granulations; but a study of microscopical section does not show this arrangement. The blood-vessels are comparatively few in number at this time, though they are much larger than those found in the surrounding parts. They have a tendency to ascend, either vertically or at a slight angle, toward the surface, where their further progress is lost. They are parallel with one another, and probably anastomose by a more or less horizontal system of capillaries in the upper layers of cells. (Fig. 44.)

The histological changes which occur during the formation of granulation tissue have already been indicated so far as the action of the cells is concerned. There is seen at first, as the result of this action, an abundant small round-cell infiltration of the part occupying nearly all the space, so that the intercellular substance is difficult to find. The fibres have, in fact, undergone a softening, and the intercellular substance appears as granular material. The majority of these cells are leucocytes which have emigrated from the blood-vessels; but many of them, principally those with single nuclei, are derived from the pre-existing cells of the part. As this tissue develops and as the cavity begins to fill, there is found, in studying with high powers, a great variety of shapes, some being club-shaped, others having a large body and a bright oval nucleus, the so-called "epithelioid cells." The epithelioid cells may be seen best near the vessels which ramify in the new tissue, and they are the principal cells relied upon for the formation of the new scar-tissue. In the deeper layers, consequently among the cells most advanced in development, are found many spindle-shaped cells running parallel with one another and in a more or less horizontal direction. This is the next stage of the process. It is between these cells that the new fibrillæ are seen forming. On the surface are found numbers of broken-down cells and polynucleated cells enclosed in a coagulated material. This is the liquefied tissue cast off from the upper layer and seen on the living granulations as pus.

The new blood-vessels form by a budding growth from the walls of pre-existing vessels. The endothelial cells of a capillary undergo division by karyokinesis, and presently there is seen a tent-like elevation (from the wall of the vessel) that continues to grow into a fine prolongation, consisting of granular protoplasm, which, after a certain length of time, contains nuclei (Fig. 47). This bud may unite with a similar one, or may return to the vessel again, forming a vascular loop, or may communicate with another vessel (Fig. 48). The vessel may also terminate in a club-shaped end. The central portion of the new protoplasm now begins to soften, and a cavity forms which subsequently communicates with the lumen of the vessel. The new tube at first has a homogeneous wall, but later the protoplasm groups itself around nuclei that are forming, and endothelium is thus developed. Some of the tissue-cells of the neighborhood come in contact with, and strengthen, the vessel-wall. When the vessels are in a state of development like this their walls are highly cellular. In all granulation tissue an active cell-growth is found near the vessel, and the endothelium of the capillaries has a special reputation for its power of procreation. This is the method of *intracellular* growth of capillaries, and is the generally-accepted theory of vascular development.

The *intercellular* method of growth is seen in the formation of a bundle of spindle-shaped cells in new tissue in which vessels are also forming. Some of these cells group themselves together, and form a channel which presently communicates directly with the vascular system. If these channels are traced carefully, the ex-

FIG. 47.—Development of Blood-vessel in Mesentery of an Embryo.

treme limits may be found to which the corpuscles have penetrated. Inasmuch as it is known that the plasma-canals are filled with blood in fresh wounds, it is highly probable that the subsequent cell-growth can form canals which open into the blood-vessels. In the writer's studies in the repair of arteries new tissue has been seen growing into a portion of a blood-vessel which has been cut off from a trunk by a double ligature, containing young vessels developing in this way. In sections of granulation tissue can be seen small blood-vessels with bands of cells branching off from their walls. In the axis of these bands the cells are separated and vessel-walls are formed from them.

When the granulation tissue has been covered with epidermis, the cell-infiltration has already in part disappeared, and the polynuclear leucocytes have broken up and have been absorbed. The fibroblasts have formed intercellular substance. Perhaps some of the fibroblasts have been transformed into fibres to awaken once more at some future time. At all events, the scar-tissue now becomes very rich in fibres, and few cells are seen there. The blood-vessels, which at first are quite numerous, and which give the characteristic redness to the new cicatrix, eventually diminish very

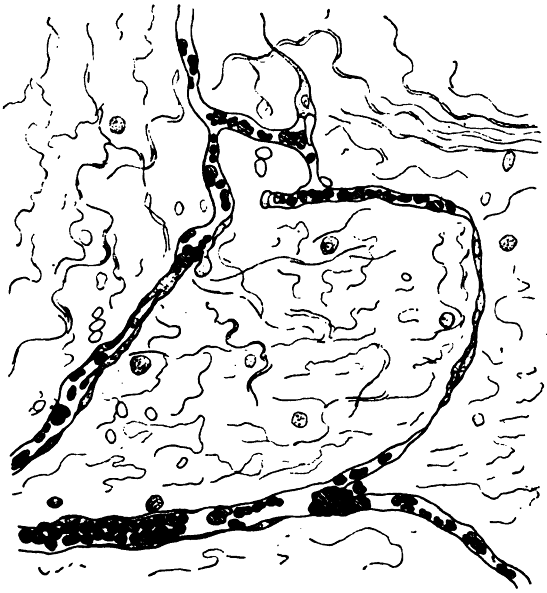

FIG. 48.—Development of Blood-vessel in Mesentery of an Embryo: formation of vascular loops.

greatly in number in the way already indicated, and the scar becomes paler than the normal skin; but this change does not occur until months after the wound has healed.

The healing of a wound whose edges have not been brought together may take place without the formation of pus, provided the cavity thus formed is filled with healthy blood-clot and the wound itself is in an aseptic condition.

The so-called *organization of the blood-clot* occurs by an ingrowth of cells into the gelatinous material thus furnished, which material takes no active part in the process, but serves as an admirable "culture-medium" for cell-development. In such cases at the end of two or three days the clot is seen filled with a round-cell infiltration, the cells of which grow more numerous as the clot breaks up and disappears. The granulation tissue thus formed, in a few days more is supplied with blood-vessels. If no suppuration takes place, a portion of the old clot remains as a scab upon the surface until cicatrization is complete. The organization of the clot is not, however, always effected in this way. In some cases the clot may recede before the advancing cell-growth, which occurs in the shape of granulations projecting in an irregular manner into it in the same way as upon a granulating surface. The clot shrinks greatly as the new tissue grows forward to take its place (Fig. 49). This method of healing by blood-clot occurs in subcutaneous wounds, in simple fractures, in ruptures of internal organs, and, in fact, to a certain extent, in almost every wound that heals without suppuration.

The granulating surfaces of open aseptic wounds (a few days old) may be brought together, and will unite by *third intention.*

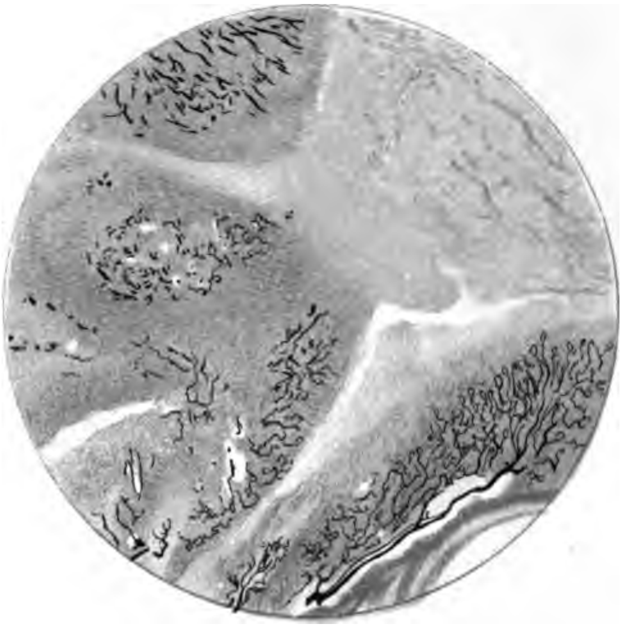

FIG. 49.—Granulations compressing Blood-clot; injected specimen (tenth day).

In older open wounds with moist and luxuriant granulating surfaces the granulations should be scraped off before bringing the edges together. In this way the healing process is sometimes greatly shortened.

The healing of tendon varies somewhat according to the presence or the absence of blood-clot. After the tendo Achillis has been divided experimentally in the rabbit, the sheath is found filled with a firm cylindrical clot. A few days later it will be evident that a growth of new tissue has taken place in the tendon-sheath, and that a callus has been formed enclosing the retracted ends of the tendon (Fig. 50). If the specimen is now removed, placed in alcohol to harden, and subsequently is divided longitudinally, it will be found that the divided ends of the tendon have retracted considerably, leaving between them a mass of blood-clot and new tissue which forms a spindle-shaped covering enclosing both ends for some distance beyond the point of division. The clot is already partially absorbed, and the new tissue is growing into it in various directions. If the limb has previously been injected with Berlin blue, the rich new formation of vessels may be seen producing a highly vascular network around the borders of the clot. In such a case as this the ordinary method of the organization of the blood-clot has not taken place, owing probably to the size of the clot, but the tissue has formed granulations which are pushing into the clot. It is probable that large clots are usually absorbed in this way by lateral pressure, rather than by infiltration with wandering cells. If the new-formed tissue be examined at this time with a high power, it will be found to consist of spindle-shaped cells running mainly in a direction parallel with the long axis of the tendon. The new tissue appears to spring from the inner wall of the sheath, while the cut edges of the tendon, standing out in bold relief, seem to take no part in the process. The new blood-vessels form about from the tenth to the fourteenth day a rich vascular network in the provisional tissue, and some of them can be seen already communicating with vessels lying between the fibres of the old tendon (Fig. 51). In the granulations which surround the margins of the blood-clot there is found a rich anastomosing network of vessels, many of them forming loop-like prolongations; others seem to terminate in club-shaped extremities (Fig. 49). The blood-corpuscles of the clot have by this time disappeared, having become pressed together, and the clot now appears as a brownish mass of tangled fibres of fibrin. As the process of repair proceeds the fusiform cells diminish in number and the intercellular substance begins to make its appearance: this process continues until a tissue is formed which, with the microscope, is difficult to distinguish from normal ten-

FIG. 50.—Healing of Tendon: callus formation with absorption of blood-clot. Granulations are seen compressing the clot from the sides, and, at the lower portion, from behind (tenth day).

don-fibre. As this new tissue develops a large portion of the provisional tissue is absorbed, together with the remains of the blood-clot, and the callus disappears.

When the blood-clot is absent the walls of the sheath come in contact, and unite as a band which joins the ends of the tendons.

FIG. 51.—Detail Study of the End of the Divided Tendon seen in Fig. 50.

New tissue in many cases grows between these walls, and a tendon-cicatrix will thus be formed.

According to Viering, the tendon-cells also take part in the repair, but no change is observed in them before the fourth day. All that is seen of the tendon-cells in the quiescent state is an elongated staff-shaped or double-oval nucleus bent into a gutter shape. There is but little protoplasm to be seen beyond a delicate granular mass around the nucleus and along the margin of the plasma-canals, on the sides of which lie these cells. The nuclei soon enlarge and the protoplasm becomes clearer. Nuclear division next takes place, and the cells soon become mingled with the fusiform cells produced by the granulation tissue. Viering also found cells which he regards as developed from the so-called "slumbering cells" in the tendon-fibres. It is probable that the tendon-cells take only a comparatively limited part in the process of repair, though the new tissue formed resembles tendon-tissue more closely when the ends of the tendon have been sufficiently approximated. In some tendons the divided ends are not reunited, owing to their great displacement. This is more likely to occur near the flexure of joints and where the sheath is lined with endothelium. Tendons widely separated may be exposed by an incision and the ends may be approximated by sutures. In this case union takes place with more or less complete restoration of function. An attempt should always be made to suture the divided ends of a tendon if there is any probability that spontaneous union will not occur. When a tendon is divided intentionally by the surgeon for the purpose of lengthening it, the ends may be allowed to remain a considerable distance apart in certain localities, as, for instance, the ankle. If it is desired to elongate the tendon of the wrist or of the hand, a plastic operation should be performed. The tendon in this case may be divided by an extremely oblique incision, so that the ends will still overlap slightly when considerable retraction of the proximal portion has occurred. A flap may be made by partially dividing one of the ends some distance above the seat of the wound, and by incising the tendon along its central axis from this point close down to the point of injury. The flap thus formed can be reflected and be united to the other end.

Repair of muscular fibre is a subject about which observers have differed greatly. It was formerly supposed that striped muscular fibres were not able to reproduce new fibres, and that the cicatrix of muscle was connective tissue. More careful histological study has disproved this view. Differences of opinion have, however, prevailed as to the origin of the muscular fibres. Some authorities believe that the new growth proceeds from the muscular cells or sarcoblasts; others assume that it originates from the contractile substance which is metamorphosed protoplasm.

Nauwerck has recently made a series of careful investigations to determine these various points, by experiments on rabbits. He found several preliminary changes which are not permanent. In small wounds of muscle at the end of twelve hours evidence of cell-division is seen in the connective tissue of the perimysium internum and in the endothelia of the small vessels. The height of the development of granulation tissue thus formed is reached about the sixth day. In the centre of this tissue necrosed fragments of muscular fibre and giant-cells are seen. This new tissue occupies the injured part, and extends along the perimysium for some little distance between the neighboring healthy muscular fibres. It does not remain long, however, and at the end of two weeks there is seen in its place connective tissue with few nuclei separating some of the muscular fibres. In the mean time, the ends of the injured muscular fibres break up into spindle-shaped fragments, and some of them undergo fatty degeneration, vacuolation, or a vesicular degeneration. Some fibres remain at first in contact with their necrosed ends; other fibres atrophy and terminate in tapering points. The separation of the necrosed fragment is favored by leucocytes and connective-tissue cells, and during the next few weeks they are gradually absorbed.

One of the earliest changes seen in the living muscular fibre is the proliferation of the muscular cells, or so-called "sarcoblasts," which appear in the form of bundles of muscular cells at the ends of the muscular fibres, either near the necrotic zone or some distance away. According to Nauwerck, they do not undergo striation, as some observers have supposed, but at the end of the first week undergo fatty degeneration, and at the beginning of the third week have disappeared. There is seen also, at an early period, a peculiar longitudinal splitting up of muscular fibres, accompanied by an active formation of nuclei, the disappearing fibre being replaced by a bundle of slender fibres having longitudinal striation and spindle-shaped cells.

About the sixth day some of the living fibres begin to elongate and to grow in among the necrosed masses of fibres. The first terminal prolongations form narrow fibres composed of a protoplasm rich in nuclei. These outgrowths occasionally surround, fork-like, a necrotic fibre. By the eighteenth day the granulation tissue is already invaded for some distance by the new fibres. These prolongations grow from the stumps of old fibres, forming the tapering fibres found near the wound, and from fibres which have been split up longitudinally. The prolongations are not always single: in some places two such growths are seen coming from one fibre, and these in turn may bifurcate. Later, these new fibres present at their ends club- or spindle-shaped swellings which are richly supplied with nuclei. Karyokinesis is seen in these nuclei, but more frequently multiplication is effected by the process of "indirect fragmentation." These muscular buds show a longitudinal striation, but by the end of the second week transverse striæ are plainly seen. The nucleated terminal portions present an appearance closely resembling giant-cells. These swollen ends disappear during the fifth or sixth week.

As the muscular fibres grow they lose their parallel arrangement and becomes entangled with one another. Budding may take place, not only from the ends of the fibres, but also laterally. The former method is, however, the usual one. The new-formed fibres gradually invade the connective-tissue cicatrix. They become thicker and cylindrical, and acquire transverse striation. Many of them do not remain permanently, but break down at an early stage of the process and undergo fatty degeneration. As the fibres grow from opposite sides of the wound they interlace with one another (Fig. 52) like the fingers of clasped hands

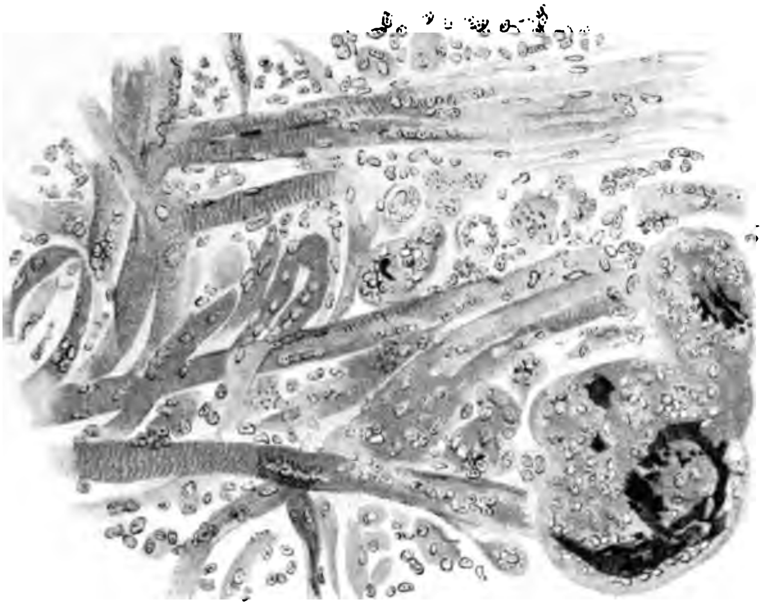

FIG. 52.—Repair of Muscular Fibre (Nauwerck).

(Neumann). In this way the connective-tissue scar disappears. In small wounds the cicatrix is therefore entirely muscular. In large wounds the fibres may be unable to form sufficient new muscle, and the connective-tissue cicatrix persists. The great irregularity in the direction of the new fibres is so modified as time goes on that the horizontal arrangement reappears, but there is usually more or less interlacing of the new muscular fibres.

Repair of Nerves.—It has now been abundantly proved that a spinal nerve when divided can reunite with return of its functional activity. It has also been proved that the perip eral end of one nerve can be united to the central end another nerve with restoration of function. As yet there a no data which show that a purely motor trunk can unite with purely sensory trunk, with a return of function to the periphe portion.

Up to the time of Nasse and Waller it was generally believ that nerves were united by the formation of new fibres betwe the divided ends, and that the peripheral end suffered no dege eration, union taking place by first intention. This view appea to have been borne out by clinical experience in certain cases which, after nerve-suture, there was an immediate return motion or of sensation, or of both. Experimental researches animals, however, have not confirmed this view. The rap reproduction of sensibility is explained in some cases by anast mosis of the peripheral branches of the divided nerve with oth sensitive nerves that have not been cut; other cases may be exan ples of the so-called "supplementary" or "vicarious sensibility and motion. The experiments of Howell and Huber, as well those of other observers, show that in animals the peripheral en of a divided nerve degenerates completely throughout its who length. There is also a degeneration of the terminal fibres the central end to a limited extent. These degenerated nerv fibres are subsequently replaced, and the repair which unites t two ends of the nerve takes place from both fragments, but chief from a downward growth of embryonic fibres from the centr portion.

The new nerve-tissue is produced from pre-existing nerve-tissu and not from the connective-tissue structures which form a com ponent part of the nerve-trunk. New nerve-fibres are conse quently not formed in the granulation tissue surrounding th ends of the divided nerve, but the actively-growing embryon fibres from the central and peripheral ends penetrate this tissu and finally meet one another and unite. According to Ranvie Kölliker, and others, the repair takes place from the central end The axis-cylinders swell and divide into several branches th eventually break through the neurilemma and ramify in the co nective-tissue structures which support the nerve-fibres (endone rium and perineurium), and cross through the granulation tissu into the peripheral end, some of the cylinders eventually findin their way into the nerve-sheaths again. In accord with this vie is the theory that the axis-cylinder is a prolongation of a nerv cell, and, when cut off, repair can take place only from the cell from which it originated.

Howell and Huber found that the return of function in the sutured nerve in a dog begins to appear on the twenty-first day, and is nearly perfect at the end of eleven weeks. This return of function cannot take place, however, without the previous degeneration of the entire peripheral end, and it is attended by a total loss of conductivity and irritability. At the end of about four days after division the continuous myeline sheath breaks up into a number of segments, and this division is accompanied by, or causes, a breaking of the axis. By the seventh day a very active proliferation of the nuclei of the nerve-sheath or neurilemma has begun. It is probable that this takes place by indirect division. After division the nuclei migrate, and several nuclei are often found in one internodal space. From the seventh to the fourteenth day absorption of the myeline takes place, together with the contained fragments of the axis-cylinder, until finally the remnants of these two substances entirely disappear.

Protoplasm now begins to accumulate around the new nuclei, and increases until a continuous band or fibre of protoplasm, in which nuclei are imbedded, is formed within the old sheath. These bands constitute the "embryonic fibres" of Neumann. After the formation of this new fibre a new sheath is made by

FIG. 53.—Changes seen in the Repair of a Nerve after Division: 1, absorption of myelin and multiplication of nuclei of nerve-sheath near points of absorption; 2, embryonic fibre six and a half months after section; 3, formation of myelin tube; 4, newly-formed myelin tube (Howell and Huber).

differentiation of the peripheral layers of this protoplasmic band, and it is supposed that the old sheath becomes part of the endoneural connective tissue (Fig. 53).

It is probable that these embryonic fibres have some of the properties of mature nerve-fibres, and that they can conduct impulses after having united with the normal fibres of the central end. Possibly this may be an explanation of the rapid return of sensation in some of the reported surgical cases.

In case the ends of the divided nerves are not reunited, the degenerative changes proceed in much the same way as when the suture has been made; but the regeneration, beginning with the formation of the embryonic fibres, proceeds more slowly than in the case of suture, and never gets beyond the embryonic stage. If the reunion with the central end has been made, the regenerative changes go on to the formation of complete nerve-fibres having myelin sheaths and axis-cylinders. It is supposed that the new myelin is formed either by a myelin degeneration of the superfluous nuclei or from the substance of the protoplasm by a process of chemical differentiation.

When the myelin sheath is first formed it encloses a core which does not take the staining by osmic acid. Neumann and others assume that the new axis-cylinder arises from this core, but Ranvier believes that one or more axes grow out from the axis of each intact fibre of the central end. In the central end the myelin and axis-cylinders disintegrate, and are absorbed for a certain distance: an embryonic fibre is formed from the new protoplasm arising from the nuclei, and in this a myelin sheath is first formed into which an axis-cylinder penetrates as an outgrowth from the end of the old axis.

It is supposed by Howell and Huber that in the normal fibre the nutrition of each internode is directly controlled by the internodal nucleus—that is, the nucleus which presides over the portion of the nerve included between the nodes of Ranvier—and that the metabolic activity of the nucleus in turn is influenced by trophic impulses received through the axis-cylinder from the nerve-centres. When the flow of impulses is interrupted the metabolisms of the nucleus and its dependent structures, myelin and internodal protoplasm, are altered, and the degenerative changes in the myelin and axis-cylinder take place. When the embryonic fibre re-establishes a communication with the central end, the protoplasm and nuclei are again brought under the influences of the trophic impulses from the nerve-centres, and consequently there is a new formation of myelin.

According to Ranvier, every nerve-fibre consists of links united together at the "points of contraction of Ranvier." Each link possesses a nucleus and represents a cell. It is evident that the protoplasm and nuclei of these cells play a prominent part in the process of repair, acting as a sort of neuroblast. It is not surprising that repair in the peripheral portion of the nerve should be effected after so extensive a degeneration, when it is remembered that changes of this kind are going on during the entire physiological life of the nerve almost as regularly, according to some authors, as the growth of epithelium (Recklinghausen).

It is evident, from what has preceded, that the connective-tissue elements play no part in the repair of nerve-tissue. The perineurium and the endoneurium throw out new connective tissue about the ends of the fragments and form a sort of callus which holds the nerve together. It is the growth from this tissue, principally, that forms the so-called "neuromata" or bulbous terminations of the ends of nerves in a stump. These tumors are really fibromata, and it is due to the contraction of the cicatricial tissue they contain that nerves thus affected are so painful.

In regard to the clinical symptoms following nerve-section it may here be said that, although paralysis following division of a motor or of a mixed nerve is immediate and complete, there are conditions, such as have already been referred to, which mask this symptom to a certain extent. Free anastomosis with an adjacent nerve will give to a certain cutaneous district a sensibility it would not otherwise possess. Another portion of the skin may receive nerve-supply from several nerves.

There is, normally, free anastomosis between the median and the ulnar nerves on the palmar aspect of the hand. It should also be remembered that there are numerous anastomoses between the musculo-cutaneous and the median nerves. The back of the hand is supplied not only by the radial and ulnar nerves, but also by other nerves. The musculo-cutaneous nerve may supply sensation to the skin of the thumb and to the radial portion of the dorsum, the posterior cutaneous nerve may supply the middle portion of the same region, and the external interosseous nerve may supply the opposing sides of the index and middle fingers.

There are, therefore, two factors to deal with in estimating the difference in duration and extension of disturbances of sensibility: first, the irregularities of nerve-distribution in individual cases, and, second, the collateral nerve-supply by anastomosis. The prognosis of nerve-suture varies greatly according to circumstances. If a nerve is immediately sutured after division and the wound heals aseptically, the conditions are most favorable for restoration of function. If there is a loss of a portion of the nerve, the prognosis is less favorable for union, and the time for repair is in such case much longer. The nearer the injury is to the origin of the nerve, the longer is the period required for repair to be completed. The restoration of function is, however, the more rapid the nearer the point of division is to the peripheral end of the nerve. Excess of inflammation tends to produce cicatricial tissue which may be dense and may interfere with the reunion of the ends of the nerve, and not infrequently it forms a bulbous termination, chiefly to the proximal end.

Old injuries are not so easily repaired as fresh injuries, as the distal portion of the nerve has undergone degenerative changes which still remain. The prognosis is not hopeless in cases in which the nerve has been divided months or even years before.

The question of repair of the nerve-tissue of the brain is one about which great doubt exists. Krebs examined two cases of brain injury—one recent, the other of long standing. Whether new cells were developed from the gray matter or neuroglia does not appear to have been definitely determined. From experiments on animals he concluded that the nerve-cells proliferated. Obersteiner says: "A divided nerve-fibre in the central nervous system is rendered permanently useless;" according to Schieffendecker, a regeneration of nerve-fibre takes place in the cords of very young animals after division, but repair is never seen in adult animals nor in man.

Nerve-suture.—There are two methods of applying nerve-suture, which are known as the *direct* and the *indirect* suture. The direct suture is applied through the nerve-tissue, but the indirect suture is passed through the perineurium only. The direct suture possesses the disadvantage of injuring the nerve-fibres that are to be relied upon for repair. It has, however, a firmer hold upon the nerve, and is therefore more reliable when there is any tension upon the suture. When the ends of the nerve can be brought together without tension the indirect suture is preferable, as it admits of a more accurate adaptation of the ends to one another.

Kölliker prefers the finest catgut, for, although silk and metal sutures do not prevent healing by first intention, it is not absolutely certain that so sensitive a tissue may not be irritated by a more permanent suture. When there is too much tension an auxiliary suture may be applied to the proximal end passing transversely to the long axis, including adjacent tissue and skin if necessary. This auxiliary suture holds the retracted proximal end in position, so that coaptation sutures may be inserted.

In primary suture the ends of the nerve should be refreshed if they have been bruised or torn. In secondary suture a fragment should always be removed from each end before they are brought together, and the bulb on the proximal end, if present, should be excised, thus removing the cicatricial tissue that has formed. In primary sutures the ends of the nerve are usually easy to find, but in secondary suture it is sometimes impossible to find one of them. When there is a considerable interval between the ends of the nerve the difficulty in bringing them together may be overcome in various ways. The simplest method, and the one which is effectual if the distance does not exceed 4 cm., is nerve-stretching. The limb should first be placed in a position favoring the approximation of the ends, and the stretching may be done with the fingers or by dressing-forceps protected by rubber tubing. Létiévant and Beach have both suggested plastic operations, the former having practised the operation upon the ulnar nerve. One or both ends are split longitudinally for some distance above the stump, and the portion thus released is reflected and united to the opposite end.

Nerve-grafting has been tested experimentally by several observers, and has been successfully performed by Landerer and Vogt on the human subject. It has been found that the implanted fragment takes no active part in the process of repair, and that the nerve-fibres undergo degeneration. It serves merely as a medium through which the nerve-fibres grow. Vanlair proposes a method called "suture tubulaire," which consists in slipping the two fragments into a piece of decalcified bone. He found, however, that the fragments occasionally grew past one another without uniting. He therefore lacerated the distal end to allow the new nerve-fibres to penetrate it. Assaky substitutes for the decalcified tubes catgut loops. The catgut sutures applied in this way are supposed to serve as guides to the growing nerve-fibres.

In very large defects or in case the proximal end cannot be found Létiévant proposed that the distal end should be implanted upon the trunk of an adjoining nerve, the trunk being opened at the point at which the nerve is sutured. When two neighboring nerves are divided, it may happen that it is only possible to bring together the distal end of one nerve with the proximal end of the other. This operation is advised in order to maintain the integrity of at least one nerve-area. Löbker in one case shortened the bone in order to bring the ends of the nerve together and at the same time to suture the tendons.

The following case is interesting in this connection: A boy entered the writer's ward at the hospital for an unreduced dislocation of the elbow-joint. Attempts at reduction failing, the joint was laid open and all bands were divided. The joint surfaces were brought in apposition, but it was then found that the ulnar nerve had been cut during the operation, and the ends were so far removed when the bones were in place that they could not be approximated. The joint was accordingly excised, and the nerve was then easily sutured. The wound healed by first intention, and at the end of two months the function of the nerve was restored and there was good motion at the elbow-joint.

Kölliker prefers, above all, the method of nerve-stretching. He places Assaky's catgut loops next in order of preference and before plastic operation, as this method follows more closely the physiological processes during repair.

Healing of Bone.—The cicatrix of bone is usually bone; that is, the bony tissue has the power of reproducing itself after injury, and it is only in exceptional cases that this does not occur.

When a long bone is broken there is a great deal of injury to the surrounding parts. The Haversian canals are ruptured, and there is a considerable oozing of blood between the bony fragments and in the surrounding tissues. This oozing is usually sufficient in amount to form a tumor of considerable size at the seat of injury immediately after the accident, and serves in many cases as a guide to the diagnosis of fracture (Fig. 54). The soft parts are also lacerated to a considerable extent. It is rare that the rupture of the periosteum does not occur. The sharp end of one or of both fragments may be thrust through the periosteum, or it may be pulled up from the ends of the bone by the displacement which takes place at the moment of injury.

FIG. 54.—Experimental Fracture (dog) at the end of the first week, showing bloodclot and detached fragment of bone.

As the result of such an injury to the part traumatic inflammation occurs at the seat of the fracture, and in a few days the tissues in the immediate neighborhood, if examined, are found infiltrated with blood-clot and are matted together by the exudation which takes place. The anatomical relations of the soft parts surrounding the bone are, for the time being, lost, and the upper and lower fragments are imbedded in an indurated mass of tissue, which, extending some distance above and below the seat of the fracture, is known as the *callus*. This callus does not have any well-defined outline, and involves not only the bone and periosteum, but also the connective tissue and some of the surrounding muscular tissue. In a few days after the injury this inflamed mass begins to take on much firmer consistency than is seen in traumatic inflammations elsewhere. If examined during the second or third week of the process of repair, the tumor is found to consist no longer of blood-clot which has been absorbed, but of a dense tissue which has formed abundantly in and beneath the periosteum, and which in places appears to have developed into cartilage (Fig. 55). A week or two later this material is transformed into a porous tissue surrounding the two fragments and holding them firmly together. In the mean time changes have been going on in the medullary canal. As the blood-clot is absorbed it is found that the fatty tissue of the canal has disappeared near the seat of the fracture, and that it is replaced by granulation tissue. Presently it is obvious that this tissue in turn has given place to newly-formed spongy bone, known as the *internal callus*. An *intermediate callus* is also recognized by some authorities as existing at this time between the ends of the bone, but it is clearly a development of bone-tissue from one of the other sources first mentioned.

FIG. 55.—Experimental Fracture (dog) after forty-six days: ossification of callus.

During this period but little change takes place in the sharply-defined ends of the shaft. Gradually, however, the dense cortical bone becomes more porous, so that at the end of one or two months a mass of spongy bone occupies the seat of the fracture. The newly-formed bone preserves the contour of the callus, forming a spindle-shaped swelling extending for some distance above and below the injury. From this time on, the new bone, formed from the medulla and the periosteum, is gradually absorbed, while the bone of one fragment, now continuous with the other, resumes its former density and becomes cortical bone once more. With the absorption of the provisional bone the medullary canal and the periosteum resume their former relations. When the fragments so overlap one another that the continuity of the medullary canal is broken a portion of the cortical bone of each fragment is eventually absorbed, and in this way the medullary canal is re-established. The object of this temporary bone-formation, known as the *provisional callus*, is to hold the broken fragments firmly together while the slow process of cicatrization in bony tissue takes place.

The histological changes which occur during the process of repair after a fracture may now be considered. Already as early as the second day there is found in the immediate neighborhood of the fracture an infiltration of the parts with leucocytes. This infiltration involves the lacerated periosteum and the connective tissue and muscular fibres. The extravasation of blood and the inflammatory exudation combine to obscure the normal anatomical structures. At some distance from the immediate neighborhood of the fracture there is found at this time an unusual activity in the deeper layers of the periosteum and in the adjacent bone. An active cell-proliferation takes place, in consequence of which fusiform cells and angular or stellate cells abound. This tissue is in intimate communication with the interior of the bone, and is, in fact, continuous with the medulla through the connective-tissue system of the Haversian canals. It has been called by Ranvier the "periosteal medulla."

In a few days there is found in this tissue a thick layer of new cells imbedded in a finely striated intercellular substance, the cells being surrounded by a halo somewhat like that seen in cartilage, and the tissue being unusually dense and firm in appearance. This is the so-called "osteoid substance." Nearer the ends of the bone, and near the centre of the inflammatory mass known as the *callus*, the intercellular substance has a more transparent hyaline appearance, and during the early period of repair this portion of the callus consists largely of cartilage.

If the osteoid substance just referred to is examined at the moment when the transformation into bone is taking place—that is, during the second or third week—it will be found that portions of this tissue take the staining fluid more readily than other portions, so that it has a more or less mottled appearance. This appearance is due to the deposit of lime-salts, and presently it is found that trabeculæ of bone have formed, and that the cells which were there before have now become bone-cells (Fig. 56). These cells are therefore known as *osteoblasts*. The spaces found between the bony plates are now seen to be in communication with the Haversian canals and to contain blood-vessels. These vessels, emerging from the canals in the cortical bone, run at

FIG. 56.—Ossification of Osteoid Substance in Callus, three weeks (dog): osteoid substance above, shaft of bone below. The dark trabeculæ are formed of newly-ossified bone; between them are the Haversian canals in process of development.

right angles to those supplying the shaft of the bone, and the grain of the new bone is consequently at right angles with that of the old (Fig. 57).

This new spongy bone is now seen forming some distance from the seat of fracture, and gradually growing thicker as the ends of the fragments are approached. As this grows out from each end of the bone, it invades the cartilaginous callus, and the two buttresses of bone developing from the ends of each fragment approach each other, and finally come together and form a bony bridge which unites the broken ends. This newly-ossified callus consists of spongy bone with a coarse meshwork, containing what might be regarded as an anastomosing network of medullary tissue. If these spaces are examined with a high power of the

FIG. 57.—Experimental Callus (dog), three weeks.

microscope, it will be found that they contain a vascular granulation tissue surrounded at the margin of the cavity by a row of cells (Fig. 58). It is evident that these cells are actively concerned in the formation of new bone, layer by layer, as the deposition of lime-salts can be seen at certain points taking place between the cells. In this way the spongy bone becomes denser and more like cortical bone. The hyaline cartilage in the specimens examined by the writer seems to be absorbed as the bony

FIG. 58.—Detail Study of Three Weeks' Callus, showing osteoblasts forming new bone.

growth shoots out from each end of the callus. The hyaline cartilage may, however, at certain points form bone by the calcification of the intercellular substance and a change of the cartilage-cells into bone-cells (Bruns). Meanwhile, in the medullary canal, near the ends of the bone, the granulation tissue becomes changed into red or embryonic marrow; osteoid substance is formed around the marrow adjacent to the cortical layer of bone, and new spongy bone is thus thrown out from the sides of the medullary canal until it is filled with a porous bony tissue. Hyaline cartilage is occasionally seen here, but this is the exception.

During all these changes the ends of the cortical bone appear to remain unaltered. The Haversian canals are filled, however, with a round-cell infiltration, and the vascular spaces are gradually enlarged by an absorption of the lime-salts, probably by the production of some chemical substance developed by the granulation-cells. The ends of the dense bone become porous, and consequently there takes place a transformation of the bone in the immediate vicinity of the fracture and the surrounding callus into a mass of spongy bone. In this way the ends of the fractured bone become firmly united to each other. This process occupies many weeks, and in some bones it may be months before the dense bony tissue undergoes the changes necessary to hold the two fragments permanently together. When union has been accomplished the callus undergoes absorption, which first occurs in the internal callus. In the medullary spaces, which again are becoming enlarged, there are found numerous giant-cells or osteoclasts that appear to play a prominent rôle in the process of absorption. The giant-cells usually lie in little excavations of the bone-substance. In this way the outer callus also is gradually absorbed, but those portions of bone that are to remain permanently become denser, and finally assume the appearance of normal cortical bone.

The amount of the callus varies greatly in different cases. It corresponds pretty closely with the amount of displacement of the fragments and with the severity of the inflammation. In ordinary cases of simple fracture the callus is found only in the angles formed by the broken ends of the bone. In animals that are allowed to run about during the process of repair the two ends of the bone are imbedded in a luxuriant callus which involves a considerable portion of the shaft.

Sometimes there appears to be an inability on the part of the bone-producing structures to form new bone. The inflammatory tissue is absorbed and no new bone is thrown out, and as a result of this there is what is called an "ununited" fracture. If the ends of the two fragments are examined, it will be found that they have lost their sharp edges by absorption of bone, and that they are now more or less pointed. The two ends of the bone are united by a ligamentous band. In some cases nature attempts to form a new joint, and it is then found that the ends are held together by a capsule which when open is seen to contain a small amount of clear serum, and the ends of the bone are covered with a more or less perfectly formed hyaline cartilage. This condition is known as *pseud-arthrosis.* In other cases the whole bone is absorbed, but this is extremely rare. The Warren Museum contains the arm of a grocer, whom the writer remembers to have seen, whose humerus was entirely absorbed after fracture. The causes that combine to produce non-union in bone do not appear to be understood thoroughly. The period of life at which an ununited fracture is commonest is, according to Bruns, between thirty and forty years. The chances of union during old age appear to be much more favorable than has generally been supposed. Individual peculiarity has probably as much to do with the development of pseudarthrosis as any other factor. Among the constitutional causes mentioned as favoring non-union are pregnancy, syphilis, scurvy, and diabetes. It is probable, however, that pregnancy exercises but little influence one way or another on the repair of bone. In syphilis it is in the later stages of the disease only that delayed union is observed.

Local causes may materially contribute to the chances of non-union. Compound fractures supply twice as many cases of non-union as simple fracture. The displacement of the fragments and the presence of anatomical structures between the ends of the bone, such as muscle, tendon, nerve, or portions of the articular capsule, are conditions that seriously interfere with union. Imperfect fixation of the fragments is also a fertile source of failure of the bones to unite. The femur and humerus, being single, are for this reason more likely to be the seat of ununited fracture than bones which are steadied by the presence of another bone. Unskilful treatment is not so frequent a cause of non-union as is supposed, but it is more likely to be followed by deformity at the seat of fracture.

Healing of Arteries.—When the trunk of a large artery is wounded an abundant hemorrhage occurs from the cut in the vessel-wall into the surrounding tissues. If there is no open wound in the integuments, a large and tense hæmatoma is formed. The blood coagulates not only outside the vessel, but also in the wound in its wall and in the interior for a greater or lesser distance. Bleeding is thus arrested and the process of repair soon begins. As the clot is gradually absorbed there is formed granulation tissue, which seals up the line of incision in the wall of the artery. The clot serves as a temporary protection against hemorrhage, but it is soon absorbed, and the cicatrix which has meanwhile formed is composed of connective tissue only, and when subjected to arterial pressure is distended until an aneurismal sac is formed.

When a *ligature is placed around a large artery in continuity*, the blood-current is permanently arrested, and it is possible for a durable cicatrix to be developed capable of resisting any strain that blood-pressure can bring to bear upon it. When the knot is firmly tied the intima and a variable portion of the media are ruptured, and the adventitia is gathered into a dense tendinous sheath around the constricted ends.

The earliest change noticed is the formation of thrombi, the distal thrombus usually being smaller than the proximal. The size of the thrombi varies greatly. In aseptic operations they are exceedingly small, but they were present in all cases examined by the writer; in fact, a thrombus was seen in the ductus arteriosus of the new-born infant, where local sepsis was highly improbable.


FIG. 59.—Carotid Artery of Horse two weeks after ligature. A callus surrounds the ends of the vessel, between which the knot may be seen. The process of repair in the arterial wall has not yet begun (specimen 1048, Warren Museum).

During the first two days granulation tissue forms about the point of ligature and for some distance above and below. This tissue also varies with the amount of traumatism; it is, however, sufficient in all cases to bury the knot. If there is much trauma or if the wound becomes septic, the amount of this surrounding inflammatory tissue is increased and a callus of considerable size is formed, which protects the vessels from the dangers of hemorrhage (Fig. 59).

If repair progresses favorably, presently the adventitia is seen invaded by leucocytes in the neighborhood of the ligature, and the infiltration goes sufficiently far to penetrate the thrombi. The solvent action of this granulation tissue gradually disintegrates the bundles of fibres surrou by the ligature, and the two ends of the vessels separate from another, leaving the knot imbedded in the centre of the ca The ends of the vessels, once released from the ligature, b to expand, and the granulation tissue penetrates freely into thrombi. Conditions are now reached closely resembling repair in fractures which have just been studied. There this stage both an external and an internal callus. With development of the granulation tissue blood-vessels are formed, which spring the vessels surrounding the ligature: t grow into the thrombi with the granul tissue, and the thrombi are then said to become "organized." The granulations develop in this way form irregular mass new tissue with spaces between them, wl when the superjacent clot is absorbed, come blood-spaces communicating with lumen of the vessel. These spaces in turn communicate with the new capillari the granulation tissue. This completes first stage of the healing process. In art of considerable size this stage is compl by the fourth or fifth week (Fig. 60).

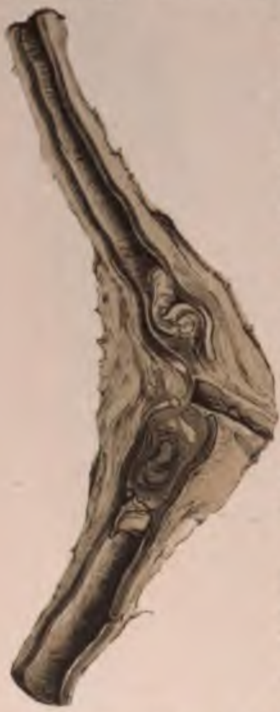

FIG. 60.—Carotid Artery of the Horse two months after ligature. The ends of the vessel have opened and the provisional tissue has grown into the thrombus. Between the ends is the ligature sinus (Specimen 1048-1, Warren Museum).

The provisional structures are now g ually absorbed, and as they disappear found that the walls of the artery have been inactive. A growth has taken pla the intima at an early stage of the pro and many of the wandering cells foun the clot come from this layer. As the and the internal callus disappear the found a permanent cicatrix, which close ends of the vessel. This cicatrix vari shape according to the presence or th sence of large arterial branches. Whe branch is present it has the shape of a cent, the horns of which project symme ally along the inner walls of the vessel. If the branch is g off on the side, the horn on that side is short, reaching onl the point of junction, while the horn on the other side pro much farther into the vessel, thus so narrowing its lumen allow it to taper gradually toward the mouth of the collateral branch.

The cicatrix, when fully developed, consists of three layers. The inner layer is composed of endothelium formed in the way already described; below this is a layer of muscular cells, developed by a proliferation of the cells of the media, and outside of all is a connective-tissue cicatrix, evidently formed by the outer walls of the vessel. There is, then, in the permanent cicatrix a reproduction of the three walls of the vessel. When the cicatrix has fully formed the provisional tissue is absorbed, and in its place is found a cord uniting the two ends of the vessel. The mass of new vessels formed in the callus has also disappeared. A small central vessel is usually seen penetrating the cicatrix from the lumen and anastomosing with a system of capillaries surrounding the end of the arterial stump (Fig. 61). In large cicatrices, which sometimes extend a considerable distance into the vessel, this central arteriole may be branched or tortuous, and may give to the cicatricial tissue a "cavernous" appearance.


FIG. 61.—Femoral Artery of Man three months after ligature, proximal end, termination of healing process. The cicatrix, composed partly of muscular cells, is penetrated by a small vessel. Below is the fibrous tissue which unites the proximal to the distal end.

The formation of a muscular cicatrix is generally denied, but the writer, having made extensive researches upon this point, is convinced that a muscular cicatrix is developed. The reason why it has not been found is easily explained. The process of permanent cicatrization is so slow that investigators have examined specimens at too early a period. The process requires a period of time varying from two to six months, or even longer, for its completion, according to the size of the vessel. Unstriped muscular cells proliferate much more frequently than is usually supposed. A physiological example of this is seen in the uterus, and every wound that unites involves a reproduction of these cells whenever new arterioles are formed.

Some writers, as Senn, and Ballance and Edwards, advise the application of two ligatures to arteries of the largest calibre when tied in continuity. They must be drawn tight enough to approximate the walls without rupturing them. The object of this manœuvre is to diminish the danger of secondary hemorrhage. When the ligature is applied in this way the ends of the vessels do not separate at once, but the vessel remains as an obliterated cord. It is probable, however, that the granulation tissue works its way into the interior of the vessel in the manner already described. This process is clearly shown in the illustrations given by Ballance and Edwards in their admirable work. There is, therefore, no essential difference in the process of repair under these circumstances. The walls of the vessel at the point of ligature are absorbed more slowly, however, and traces of them probably remain here and there in the cord uniting the two ends of the vessel.

The old idea that the thrombus was organized is now so generally abandoned that it is unnecessary here to discuss the question. The rôle of the thrombus is protective. In aseptic cases it is reduced to a minimum. In septic cases the whole length of a long trunk may be plugged by a clot.

After the ligature of an artery in an amputation-stump the process of repair goes on in the manner described, but there are certain important modifications in it to adapt the circulation of the blood to the new conditions. The main artery of the stump so contracts that its calibre is greatly diminished. The cicatricial tissue which forms extends a long distance into the interior of the vessel, sometimes even throughout its whole extent. In this way its size is further diminished, so as to adapt it to the greatly diminished blood-supply needed for the part. The collateral branches increase in size, so that finally, instead of a large vessel ending abruptly as a cul-de-sac at the end of an amputation stump, there is a much smaller vessel which terminates in a large number of branches distributed in various directions. This diminution in the lumen of the main trunk is analogous to the change which occurs in the hypogastric arteries after birth. There is a so-called "compensatory endarteritis," which in the new-born infant involves even the aorta. The changes seen after ligature in continuity are analogous to those which follow obliteration of the ductus arteriosus. In both a substantial muscular cicatrix is secured at the point of obstruction to the blood-flow.

In closing, a word about the ligature. Scarcely any subject in surgery has caused more discussion. Ligatures, usually of silk, were at first left with one long end, so that they could be withdrawn when they had cut their way through the vessel. This method was disadvantageous, as the ligature kept the wound open. Acupressure and torsion were substituted, but they were soon supplanted by animal ligatures, which are absorbed. Since it has been understood that silk ligatures can be made aseptic, they are now used by most surgeons, as animal ligatures may become absorbed too soon, and a feeling justly exists that they are not to be relied upon. The proposition to apply two ligatures in such a way as to approximate the walls of a vessel without rupturing them is not likely to come into general favor. This method has not the merit of simplicity, and by it the dangers of suppuration are increased. If a ligature is not firmly applied, the lumen of the vessel may not be occluded. It is true that there is danger that the first half of the knot may loosen while the second half is being tied, and this accident has occasionally occurred, but its danger may be obviated by extra care in the application of the ligature. The old idea that the inner coats must be ruptured should no longer influence the surgeon. He should simply endeavor to place the ligature firmly enough upon the vessel to occlude it. A rough hempen or a braided-silk ligature may be needed to hold the first half of the knot in the largest arteries. In all other vessels the slipping of the knot need not be taken into account. Secondary hemorrhage after the ligature of arteries in continuity has become an accident of extreme rarity since the introduction of aseptic surgery.

X. GANGRENE.

NECROSIS is the term usually employed by pathologists to denote death of a circumscribed portion of tissue. This term is comprehensive in its significance and is applicable to all forms of local death. It is, however, usually limited to death of portions of internal organs where, owing to the absence of bacteria, putrefaction does not take place and the dead mass is absorbed, new tissue growing in from the surrounding parts to form a cicatrix. *Gangrene* is a term applied to death of a part on the surface of the body, which part is readily accessible to bacteria, and therefore almost invariably is accompanied by decomposition. *Mortification* and *sphacelus* are terms also used to denote this variety of gangrene. Surgical custom has limited the use of the term "necrosis" to death of bone: it will be necessary, however, to employ the term in speaking of the death of portions of internal organs.

The *causes* that produce death of a part are usually divided into three groups: the first group includes those causes which act directly upon the tissues by mechanical or chemical action, as when a part is crushed by violence or when a powerful escharotic is applied to the surface of the body; in the second group are those forms of gangrene caused by thermic agencies (exposure to a temperature of 54°–68° C. will produce death of a part, and cold, —16° C., will also bring about a similar result); in the third group are those forms caused by a deprivation of the nutrition of the part, as when the blood-supply is cut off by the obstruction of a blood-vessel. Gangrene may be caused by the action of bacteria, either through the specific chemical substances which they liberate, or as the result of vascular obstruction due to the inflammatory process to which they give rise.

A neuropathic form of gangrene has been described by several authors, who assume that the injury of the so-called "trophic nerves" is the cause of death of the part. The readiness with which decubitus, or bed-sore, appears after injury to the spinal cord is strongly suggestive of such a theory. Samuel calls attention to the fact that in spinal and cerebral affections the presence of skin rubbing against skin may be sufficient to produce gangrene, as on the labia and the scrotum, and that large doses of chloral administered to the insane cause profound sleep, during which in one night decubitus may be produced. It is, however, probable that the complete immobility of the paralyzed part and the simultaneous alterations in the innervation of the nutritive blood-vessels are sufficient to account for the changes produced, without assuming the presence of a special set of trophic nerves. Gangrene may, however, be caused by the action of the vaso-motor nerves, as will be seen later. The condition of the nutrition of the tissues is also an important factor in the development of gangrene. In old and feeble individuals, in whom the circulation is impaired by weak heart-action or as the result of fever of a low type, gangrene follows readily upon slight injuries. Individuals affected with diabetes or with scurvy are peculiarly liable to gangrenous processes. The so-called "marasmic thrombi" are due usually to a slowing of the current and a coincident defect in the walls of the blood-vessels, thus favoring the coagulation of the blood.

One of the first *changes noticeable in the tissues* after death of the part is the disappearance of the nuclei of the cells. In some cases chromatin (or the substances which take the staining most readily) collects in the form of granules, and is removed from the nucleus into the protoplasm of the cell, where it is dissolved and disappears. In other cases the nucleus itself loses its power of taking the staining fluid, is dissolved, and disappears. Such changes are readily seen in the epithelium of the kidney after embolism of a vessel: at the same time the affected tissue has a pale, cloudy, yellowish-white appearance, readily discernible by the naked eye.

If the necrosed tissue contains substances capable of coagulation as well as the ferment necessary for coagulation, and if there are no processes, such as suppuration, unfavorable to this change, there may arise the condition described by Weigert as coagulation-necrosis. This condition is not unlike that which occurs when blood coagulates and a thrombus is formed. The cells of the tissue become altered to granular or hyaline masses and lose their nuclei. The intercellular substance also undergoes a hyaline degeneration. A striking example of this change is seen in muscular fibre when necrosis occurs as the result of trauma or of toxic infection or a burn. The connective-tissue fibres swell up and run together as a homogeneous mass. The dead tissues have a grayish-white color, or they may be tinged a dirty brown by the admixture of blood; a greenish-gray color indicates the beginning of decomposition.

Recklinghausen has observed the formation of *hyaline thrombi* in the arterioles, and occasionally in the capillary vessels of gangrenous parts. The hyaline masses appear homogeneous and, rarely, slightly striated, and fill only partially the lumen of the vessel. They appear to be formed during the contraction of the arteries, and to be connected in some way with changes in the arterial wall. In some cases the walls themselves of the capillaries undergo a hyaline degeneration. These conditions have been observed in senile gangrene following burns, and in gangrene produced artificially in a cock's comb by the administration of spurred rye.

Gangrene is in many cases so intimately connected with *changes in the arterial system* that it is necessary to refer briefly to some of the forms of arterial disease that are liable to produce it. The inflammation of the walls of arteries is almost invariably accompanied by the formation of new tissue—a condition which has an important bearing upon the circulation through the diseased channels. In the aorta an inflammation of the intima is accompanied by the production of warty, sometimes pediculated, growths which project into the lumen of the vessel. In the small arteries this growth from the intima involves a vessel through a considerable portion of its length, and it may be so extensive as to fill out the greater part of the lumen, producing a condition known as *obliterating endarteritis* (Fig. 62). This new formation is developed chiefly from the endothelium. Later, when the new tissue has developed to a considerable extent, new vessels form in it which spring from the vasa vasorum. Many of them also communicate directly with the lumen of the vessel. It is by means of these vessels, some of which are of considerable size, that the circulation is maintained. They are not mere blood-channels, but are supplied with a wall of their own. In cases where such extensive changes have taken place

FIG. 62.—Tibial Artery from a case of Senile Gangrene of the Foot (obliterative endarteritis).

it will be found that also both the middle and the outer coats of the artery are involved in the inflammatory process.

In many cases the inflammation terminates in atheromatous degeneration of the walls of the artery. In this case the beginning of the process is characterized by the formation on the inner wall of soft gelatinous nodules, which later become of almost cartilaginous hardness, the result of a growth from the intima. Later the media and the adventitia become involved, and there is next discovered that degenerative or atheromatous changes are beginning, and when the nodules are laid open with the knife they are found to contain whitish and yellowish masses even in their deepest portions. As these masses soften the surface of the nodules becomes involved and an atheromatous ulcer is formed. If, however, the focus of degeneration is more deeply seated in the wall of the vessel, a cavity is developed containing fatty granules, cholesterin crystals, and fragments of tissue, forming the so-called "atheromatous abscess" (Orth). These little abscesses may eventually break and discharge their contents into the interior of the vessel. Such crateriform ulcers offer an opportunity for the development of a thrombus. In the heart or the aorta such a clot would furnish the point of departure for an embolus. In the smaller vessels these formations lead to the obliteration of the lumen. These abscesses may heal and leave scars. In some of the atheromatous foci calcification may take place. These calcareous masses may be present in large numbers in the aorta covered by epithelium, or they may be found projecting from atheromatous ulcers. Their size and shape indicate that they have developed from the calcification of thrombi which have been deposited on the wall of the vessel. When all these various changes are present in different stages of development there exists the condition to which the name "endarteritis deformans" has appropriately been given.

The pathological changes produced in the wall of the artery by syphilis, and even by tubercle, are also sufficient to impair their function of nutrition. The effect of the changes in the arterial circulation must of course be great. Occurring as they do chiefly in advanced life, they are accompanied by great enfeeblement of the circulation at the extremities. If the arterial disease has been in the smaller vessels, the diminution of the force of the circulation is gradual, and absolute cessation is finally brought about either by the formation of a small thrombus or by some slight injury. The arterial supply being cut off, no fluid is brought to the dead part, and the veins, being unobstructed, have not retained any venous blood in the part, consequently the part becomes gradually dried by evaporation and the form known as "dry" or senile gangrene is produced. The coloring matter of the retained blood, being diffused through the dead tissues, imparts to them the characteristic dark color of this form of gangrene. The dried tissues eventually become hardened to a leather-like consistency; hence the term *mummification*.

When there is sudden arrest of the arterial circulation or death of the part through venous obstruction, there exists the condition known as *moist gangrene*. Bacterial infection soon brings about decomposition, during which gases are often developed, producing emphysema of the tissues. The blood-corpuscles are soon broken up and dissolved, and the cells become cloudy, lose their nuclei, and break down. The striations of muscular fibre disappear, and the mucin of the nerve-fibres runs into drops. Fat-cells become disorganized, and drops of fat are mingled with the swollen and softened fibres of connective tissue. In this way the tissues gradually become dissolved.

While these changes are going on, the surrounding healthy tissue undergoes a reactive inflammation, due to the putrefactive changes which are developing in the gangrenous part. A red line of inflammation is formed at the point where the gangrene has ceased to spread, and the dark, discolored dead masses stand out in strong contrast to the bright-red color of the inflamed tissues about them. In this way the so-called "*line of demarcation*" is formed. When suppuration takes place the dead tissue becomes separated from the living, and the gangrenous tissue is in this way eventually liberated.

In necrosis of internal organs, of which infarction of the kidneys or of the lungs is an example, there is rarely bacterial infection, and suppuration does not take place. There is, of course, no line of demarcation in such cases, but the living tissues grow into and replace the dead substance, which is gradually absorbed.

Senile gangrene occurs most frequently in people over fifty years of age, and is caused, as before stated, by arterial disease. Death of the part may take place from a thrombosis of the small vessels or in the arteries leading to it, or it may be due to an embolus. The immediate cause of gangrene is often a weakening of the heart's action in an individual in whom, owing to the conditions mentioned, the peripheral circulation is already very feeble. A slight injury, like the bruising of the foot or even a "hang-nail," may be the starting-point of the disease.

The part most frequently attacked is the foot, one or several of the toes being affected, it being extremely rare to find the disease in the upper extremities. The earliest symptom is redness and swelling of one of the toes, accompanied sometimes with considerable pain. This condition is very apt to be mistaken for an attack of gout. The characteristic discoloration, however, appears and settles the diagnosis. It usually involves the whole toe, but does not spread beyond. A line of demarcation forms at the metatarso-phalangeal articulation, and the toe shrinks or it becomes coal-black in color, and the integuments become dry and wrinkled, and sometimes almost as hard as wood. The pain has by this time ceased, and the patient's general condition may not be materially affected. In favorable cases the toe is gradually separated and falls off, and the wound heals by granulation. In many cases, however, the attempt of nature to form a line of demarcation fails and the gangrene spreads to one or more adjacent toes. The surrounding tissues are now in a state of inflammation, as there is more or less decomposition in the gangrenous part, owing to the presence of bacteria, and their bright-red color is in strong contrast to the blackened toes. If the gangrene does not spread, a line of demarcation forms along the border of the dead part, but the disturbing influences of septic inflammation are in many cases sufficient to continue the process. Many of the bacteria form substances having an escharotic action upon the adjacent tissue, and the nutrition of the neighboring parts must be in good order to enable the tissue to resist them. When gangrene has once reached as far as the dorsum of the foot, the prognosis becomes very grave, and the patient, after nature has made several vain attempts to form a line of demarcation, dies of exhaustion at the end of a prolonged illness. In such cases as this it usually will be found at the autopsy that the tibial arteries have been involved in an obliterating inflammation or that their walls are rigid and atheromatous. There is, therefore, the danger that the gangrene may also involve the leg as far as the knee, and this is occasionally the case where an extensive thrombus has formed throughout the length of these vessels, extending even into the popliteal and femoral arteries.

Haidenhain, in a careful examination of a number of legs amputated for senile gangrene, found evidences of thrombosis either of the femoral artery or of its branches. In 11 out of 20 cases there was almost complete obliteration of the larger vessels by old thrombi, many of which had already become organized. According to this writer, thrombi form at the point of bifurcation of the popliteal and fill the tibials in their whole length. Such thrombi were found quite often in diabetic cases.

Gangrene of the foot and leg combined is, however, more often due to embolism than thrombus. Here the onset is more acute, and generally occurs in an individual who has had signs of previously existing heart or arterial disease. The first symptom may be a sharp pain in the foot and the calf of the leg, and when seen early the affected portion of the limb is blanched and cold and pulsation in the tibial artery is absent. Such a group of symptoms in an individual with a history of cardiac disease places the diagnosis beyond a doubt. The most frequent point of lodgment of such an embolus is the bifurcation of the popliteal artery. A thrombus forms immediately upon the proximal side of the embolus, and the femoral artery may be obliterated for a considerable portion of its length. The following cases of embolism of the popliteal artery will serve to illustrate the clinical features of this affection:

In one case, a hospital patient, the leg was removed just below the knee-joint, and the patient made a good recovery. In another case embolism occurred in a patient affected with heart disease after a very exhausting political campaign. The limb when first seen was cold and pulseless ; the patient had suffered a great deal of pain for twenty-four hours. The pulse was rapid and intermittent and the general condition of the patient was bad. Amputation was performed on the third day, after an attempt had been made to improve the patient's strength. By this time the limb had become discolored for some distance above the ankle, but the muscles and the skin of the calf still retained a natural color. Amputation was performed at the lower third of the thigh, and the vessels were found plugged with thrombi, so that there was no hemorrhage. A large fresh thrombus projected from the femoral artery, and it seemed to extend into the vessel for a long distance. Slight sloughing of the flaps and connective tissue of the interior of the wound occurred a few days later, but the sloughs eventually separated and were replaced by healthy granulations. A week after the operation a sharp pain occurred in the chest, with a rise of temperature, followed by the expectoration of a dark clot, indicating the development of an infarction of the lung. The patient died three months later of an infarction of the spleen, which suppurated, a large abscess being found in this region at the autopsy.

Embolism of the brachial artery may also occur, but not so frequently as in the femoral artery and its branches.

Treatment.—In the mildest cases of senile gangrene, when one toe only is involved, it is advisable to refrain from interference. The metatarso-phalangeal articulation lies deep, and meddlesome surgery may cause the gangrenous process to extend. In the student days of the writer this old surgical rule existed—namely, that in spontaneous, or idiopathic, gangrene, as it is often called, the surgeon should wait for the line of demarcation, but that in traumatic gangrene he should amputate at once.

The mortality following conservative treatment in senile gangrene was, however, so large that the old rule has been abandoned, and it is now advised by the best authority to interfere as soon as it is evident that there is not sufficient power to form a line of demarcation. A good rule to follow is to advise amputation as soon as the gangrene has invaded the sole or the dorsum of the foot, for it is then liable to spread with much greater rapidity. The point at which amputation should be performed is a question about which authorities differ. As has been seen, the tibial arteries are usually diseased in their entire length, and the circulation in them is therefore almost always more or less diminished. For this reason many surgeons prefer to amputate above or below the knee-joint; that is, at a point well removed from the region of the disease. In one case the writer operated with good results, on a feeble individual who had diabetes, at the middle of the leg, but if the strength of the patient will bear it, it is better to amputate at the lower third of the thigh.

Before undertaking to interfere surgically it is well to ascertain the probability of similar processes occurring in other portions of the body, as the following case will show:

A man fifty years of age, but in appearance much older, entered the hospital with gangrene of the great toe and a portion of the same foot. He had injured it two months before in very cold weather. The leg was amputated a few days later at the point of election. The patient recovered from the operation and the wound healed well during two weeks, but he died on the seventeenth day after three days of severe illness. At the autopsy there were found, in addition to an obliterating endarteritis of the tibial arteries with calcification, obliteration of the splenic artery, thrombosis of the splenic vein, and anæmic necrosis of the liver and spleen. The immediate cause of death was thrombosis of the femoral vein and pulmonary artery.

The amount of disease in this case was such as to make it doubtful whether an amputation should have been attempted with much hope of success. In case a conservative treatment is decided upon, careful attention should be given to the patient's general condition. Cardiac tonics and a nourishing diet with stimulants are indicated. The parts should be kept in as antiseptic a condition as possible, and every opportunity should be given to the gangrenous toes to become mummified. In case of embolism an effort should be made to save the limb. The parts should be elevated slightly to favor venous circulation, and be encased in warm cotton, care being taken to avoid all constriction of the circulation by the dressings. When once the diagnosis and the extent of the gangrene are established, the sooner amputation is performed the better.

A condition very closely allied to senile gangrene is that known as *diabetic gangrene* (Pl. III.), which occurs also in elderly individuals. It is important, therefore, that the condition of the urine should be carefully determined in all cases of senile gangrene. The picture of the disease so closely resembles that already given that there is little to add to it. Furuncle and carbuncle, bed-sores, pneumonia, abscess, and gangrene of the lungs also occur in diabetic patients. Diabetic individuals bear surgical operations so poorly that in general it is the custom to advise against operations in persons affected with this condition of the system. The writer would not, however, hesitate to advise amputation in a case of spreading gangrene.

A gentleman sixty years of age applied to the writer for treatment of gangrene of the third toe of the left foot. The right leg had been amputated two years previously for gangrene. There was found well-marked diabetes, and when the gangrene began to spread to the foot amputation was performed in the middle third of the leg with a successful result. There was marked atheroma of both tibial arteries. By careful attention to diet the patient recovered his strength, and when seen by the writer a year or two later appeared to be in excellent health.

Haidenhain in a recent article undertakes to show that gangrene in diabetes is due to arterio-sclerosis of the vessels, as in senile gangrene, and advises amputation at the thigh as soon as the gangrene has invaded the sole or the dorsum of the foot. Of 13 cases of amputation below the knee, including disarticulation of toes, Chopart's and Lisfranc's amputations, and amputation of the leg, only 2 recovered; 2 cases died from gangrene of the flaps, and later, in 9 cases, amputation was made at or above the knee. Of 27 primary and secondary operations above the knee, 19 cases were cured and 8 died of diabetic coma. In none of these cases did the condition of the wound appear to be the cause of death. Haidenhain advises the cutting of very shallow flaps.

It is customary to describe *moist gangrene* as a separate variety, but many cases of senile gangrene may be moist, this condition depending in such cases on the rapidity with which the disease has established itself and on the amount of tissue involved. A frequent cause of moist gangrene is injury to the large vessels by gunshot wounds or the complications which result from fractures.

PLATE III.

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Diabetic Gangrene.

PLATE IV.

W. J. KAULA, DEL.

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Gangrene of Leg, following ligature of femoral artery for popliteal aneurism.

Traumatic gangrene is almost always of the moist variety. Gangrene of this type may occur also from acute inflammation and from burns and frost-bite. Obstruction to the venous circulation from thrombosis or from pressure by bandages or dressing will retain the fluids of the body in the part and prevent any tendency to mummification. As examples of venous obstruction there may be cited strangulated hernia and severe forms of paraphimosis. The sloughing of flaps after an amputation for injury is also an example of moist gangrene.

The characteristic appearances of the traumatic form of moist gangrene are best seen after an injury to some large vessel, such as the popliteal or the brachial artery (Pl. IV.). For the first twenty-four hours it is doubtful whether the limb will live or not. Pulsation of the tibial (if the lower extremity is the injured member) is wanting from the beginning. The limb is blanched and is colder than the opposite limb. The patient, who has suffered from the pain of the original lesion, is relieved of pain with the approaching death of the limb; and, inasmuch as he is still able to move his toes, he fails to appreciate the grave nature of his injury.

The skin discoloration which begins at the end of twenty-four hours is usually a symptom that may be relied upon as characteristic, but extensive ecchymosis may sometimes give a misleading impression. The writer well remembers a case of frost-bite where the greater portion of both feet were of a coal-black hue: he obtained the patient's consent to a double amputation above the ankle, but at the moment of the administration of ether doubts as to the propriety of operating determined him to wait another day. The patient eventually escaped with the loss of one or two toes of each foot.

The irregular distribution of color shows that the circulation has been greatly impeded, and livid spots alternating with an unusual pallor are more certain indications of approaching gangrene. When decomposition sets in a greenish tinge is added to the variegated coloring of the limb. The part now becomes swollen and of a soft, unnatural, pulpy consistency. Pressure fails to bring about a paleness of the skin with a subsequent return of color. Blisters filled with a bloody serum form upon the surface. The swelling and discoloration are partly due to increased blood-pressure in some of the vessels of the part, for there is still a limited circulation in the veins even when mortification has set in. At this period there is an entire loss of sensation in the part, and the patient will bear the prick of the scalpel without flinching. In many cases it is only by some such demonstration as this that he is convinced that there is no longer need of an attempt to save the leg. In favorable cases the gangrene is confined to the injured part, and in this case a line of demarcation forms, but even before this line shows itself it becomes evident from the contrast between the white healthy skin and the swollen and discolored tissues that the gangrene will not spread. The color deepens in hue, and becomes eventually either dark green or coal black. The tendency of the deeper parts to soften is very marked, and muscular tissue soon becomes reduced to the consistence of a brick-dust paste. Tougher tissues, like tendons, retain their form much longer, and bone is rarely altered by the gangrenous process.

When the putrefactive changes are more acute, the chemical changes are probably brought about by more malignant forms of bacteria, as the streptococcus or malignant œdema bacillus. The saprogenic organisms also play a prominent rôle. In such cases the gangrene readily spreads, and it is accompanied by the formation of gases which spread through the loose tissue in advance of the disease. These gases consist of ammonia, sulphide of ammonium, sulphuretted hydrogen, and volatile fatty acids. In the foul, discolored, and greasy fluids that ooze from the wound there are found leucin, tyrosin and fat-crystals, crystals of triple phosphate, and clumps of dark pigment. The gangrene rapidly spreads, and while the patient is endeavoring to make up his mind to the loss of a foot the whole limb may be destroyed. The changes of color in the skin are rapid and striking in their effects. The part is dark green or black, the leg a livid bronze color, and streaks of green and bronze run in long narrow bands up the thigh. The constitutional disturbance is profound. The patient suffers from acute septicæmia; there are collapse with a small and frequent pulse, rapid respiration, profuse perspiration, and choleraic discharges from the bowels. The citation here of a few cases will serve to indicate the grave nature of the affection:

A man was shot through the leg by a discharge from a fowling-piece, the posterior tibial artery being lacerated in its lower third. Pulsation could not be felt in the artery at the ankle-joint. An attempt was made to save the limb. On the third day the foot became gangrenous, and the disease spread so rapidly that twenty-four hours later amputation at the junction of the middle and upper third of the thigh failed to save his life. The whole limb was in a state of acute putrefaction, being distended with gas and emitting a foul odor. The skin presented a variegated coloring of green, brown, bronze, and black.

An elderly woman addicted to the use of alcohol fell and sustained a compound Colles' fracture, the sharp edge of the shaft of the radius piercing the radial artery. When seen a few days later the arm was swollen above the elbow and was greatly discolored; the hand was closed, claw-like, and greatly swollen. A foul discharge oozed from the wound. Amputation was performed at the middle of the arm. The softer tissues of the gangrenous portion were almost completely macerated. The patient made a good recovery.

A boy fifteen years of age sustained a fracture of the bones of the forearm while trying to vault over a bale of goods. The patient was brought into the hospital a few days later with the forearm in splints and in a gangrenous condition. The next day the arm was much swollen and discolored, and of a deep bronze hue. Emphysema could be felt over the shoulder and the corresponding half of the chest. There being no wound through which decomposing fluids and gases could escape, a number of free incisions were made in the parts already dead to relieve the tension and favor drainage. In this way the spread of the gangrene was arrested, and the next day a line of demarcation formed below the shoulder-joint, and the boy eventually recovered.

These cases of traumatic gangrene require the most prompt interference on the part of the surgeon. They are known as "fulminating gangrene" or "gangrenous emphysema," or, in the expressive French language, as *gangrène foudroyante*.

Gangrene may result from some of the forms of inflammation with intense congestion of the parts. In some cases of hyperæmia accompanying inflammation there is, as has already been seen, a slowing of the blood in the capillaries, and in this condition red corpuscles are often forced through the walls of the vessels, giving rise to the hemorrhagic type. This degree of congestion precedes total stasis, which, when it occurs on a large enough scale, produces death of the part. But death is still more frequently caused by the direct poisonous action of bacteria. When an inflammation is about to terminate in gangrene, the bright red color becomes a deep livid red, mottled with blue, later a purple hue, and finally black. The underlying tissues are boggy and are distended with gas and decomposed fluids. There is great swelling of the adjacent lymphatic glands. At the seat of the lesion the muscles and tendons are macerated, the bone is denuded and surrounded by a putrid fluid mingled with pus. It is in this fluid that one finds the largest number of micro-organisms. The constitutional disturbance is profound. There is great physical prostration and the signs of septicæmia are well marked. A post-mortem examination shows that the viscera are congested and œdematous, and present hemorrhagic infarctions (Park).

Such gangrenous types of inflammation occur only from some of the most poisonous forms of bacterial infection, as, for example, the bacillus of malignant œdema. Occasionally a man is brought into the hospital with an entire arm in this condition, the result of an acute phlegmonous inflammation arising from a poisoned wound in the hand. The infection occurs often after the most trivial lesions, as the prick of some dirty tool or instrument.

The treatment of moist gangrene varies greatly according to the conditions under which it develops. The old rule, to amputate at once in traumatic gangrene, has but few exceptions. If there is no tendency to spread, a time can be chosen for the operation when the condition of the patient is satisfactory to the surgeon. In spreading gangrene the loss even of hours is sometimes fatal to life. There are but few cases in surgery that are more urgent than these. Free incisions may sometimes relieve tension and permit the escape of foul gases and fluids, but such a resort is not to be depended upon to arrest the process, and it should only be employed when amputation is not permissible on account of the low state of the patient. The process, once fully developed, may leave the patient in such a state that life can only be saved by amputation.

It is hardly necessary here to remind the reader that good food and stimulants, both alcoholic and cardiac, may be needed to develop all the strength which the system can command. Alcoholic stimulation is about the only form of treatment that can be depended upon in this grave condition.

Gangrene from frost-bite may result partly from the effects of cold and partly from the enfeebled condition of the patient. A temperature of —16° C. is sufficiently low to produce this condition. Exposure to cold in a drunken sleep is the commonest way in which this form of gangrene is acquired. The parts—usually the feet—at first are blanched, and later become purple or marbled, running in shade from a deep black in the toes to a mottled purple which may extend above the ankles.

The effect of cold upon the small arteries is to cause them to contract to prevent the flow of blood. If this condition of spasm is maintained too long, the arteries will not dilate and the blood will never return. If kept up for a certain length of time, they will dilate to such an extent that the part will become engorged with blood, and gangrene may be produced in the same way as in the acute congestion described above. There will be an intense passive hyperæmia with stasis in the vessels, that may lead to death of the part or to a chronic inflammatory process. The blood must therefore be allowed to come back gradually, and it is for this reason that treatment by cold is so often used. The Esquimaux place a frozen man in a room at the temperature of zero Fahrenheit, and gradually raise the temperature to the desired point. The practice of bringing a case of frozen feet into the warm ward of a hospital should, if possible, be avoided. The part, at all events, should be kept in an atmosphere cooled by ice-bags while the skin is kept dry. Usually the threatening color will gradually disappear, or will prove to be due chiefly to extravasated blood beneath the epidermis, and the gangrene will be found quite limited in extent.

The use of poultices to warm the dead parts should be avoided, as they promote suppuration and favor burrowing of pus. After the warmth has fully been restored an antiseptic dressing should be

FIG. 63.—Gangrene of the Toes from Frost-bite.

applied until the line of demarcation is established, when the dead parts can be removed by an operation if necessary (Fig. 63).

A not uncommon cause of gangrene is extravasation of urine.

The effect of an ammoniacal urine laden with bacteria is to cause an extensive slough of the connective tissue and occasionally of the scrotum. Free and early incisions are indicated in such cases. When a portion of the scrotum becomes gangrenous and separates, the remainder retracts, and the loss of integument appears to be much greater than it really is. Although the testicles and cords may be exposed in their entire length, they will eventually be covered in by the granulating wound. The treatment of such cases consists in free incisions through the whole extent of the extravasated area. An incision on the median line, dividing the scrotum into halves as far down as the point of rupture in the urethra, is usually called for.

A rare occurrence, which the writer has seen only once, is gangrene of the urethra and glans penis due to obstruction of its nutrient artery. In this case the gangrenous parts were carefully dissected away and a clean external wound was left, but the patient succumbed to a gangrenous cystitis.

Noma, or *cancrum oris*, is the result of gangrenous stomatitis affecting the cheek. Noma occurs most frequently as a complication of one of the eruptive diseases of children, such as scarlet fever; it may also affect the pudenda. It is evidently produced by a septic inflammation, although Samuel regards it of neurotic origin, as it does not pass the middle line and is developed without preceding inflammatory symptoms. Schimmelbusch has examined one case for bacteria, and found small bacilli, often in pairs and sometimes in long filaments, growing along the boundary-line of the living tissue. These bacilli grow in gelatin without liquefying it at the temperature of the room, and injected into rabbits they cause abscesses. They did not stain by Gram's method. Lingard examined five cases and found a bacillus 4–8μ long; when injected into rabbits it caused inflammation, and death on the tenth day.

Foote examined one case of noma and found bacilli, but he failed to obtain cultures of them. Sections taken from the skin at the edge of the ulcer covering the malar bone, and stained by Gram's method, showed an outer zone of necrotic tissue and an inner zone of normal tissue. At the edge of the necrotic zone bacilli were found packed closely together to the exclusion of all other bacteria along the line of necrosis: this gave the impression that they were eating directly into the sound tissue. They were, in fact, seen infiltrating the healthy connective tissues, though in much less abundance than along the line of necrosis. Thus far, there is not sufficient evidence to show that an organism which may be regarded as specific has been obtained by a number of independent observers.

The cheek is usually affected, and the loss of substance is so extensive that the whole side of the mouth is frequently exposed. The bones of the superior and inferior maxilla may be laid bare, and the teeth may frequently drop out. After the slough has separated the wound appears like a sharply-cut gigantic ulcer, involving the side of the nose and the entire cheek. After cicatrization takes place a large opening still remains, and the case requires an elaborate plastic operation for its relief. At the pudenda the disease usually begins at the labial margin and extends to the clitoris, the nymphæ, and the hymen, and sometimes to the urethra. The disease may spread to the perineum, to the anus, or to the thigh (Hamilton), and, as in the mouth, the sloughing is deep and frequently extends quite to the bone.

The constitutional treatment in noma is of the greatest importance, and it is chiefly through this treatment that life may be saved. Quinine and iron may be given in full doses, and stimulants also. Disinfecting gargles may be used for the mouth and antiseptic dressings for the pudenda. A few drops of an emulsion of styrone ʒss, glycerin ʒiv, water ℥iij, added to a glass of water, forms an agreeable and efficient disinfectant for the mouth. In the use of antiseptics care should be taken to avoid poisoning by the absorption of the drugs used.

Ergotism, or gangrene produced by eating grain containing ergot of rye (*Secale cornutum*), was a disease of the seventeenth and eighteenth centuries, and at one time produced great havoc among the farmers in France, Switzerland, and other countries of Europe. It has been denied that the drug could produce this effect when used experimentally upon animals; but according to Recklinghausen the characteristic effect was produced in a cock's comb, where a spasm of the arterioles was observed after its administration, and the contractions were severe in degree and of long duration. At one time the mortality of ergotism is said to have been very great, entire hands and even whole limbs being affected by the gangrenous process.

Decubitus, or bed-sore, is a form of gangrene produced by pressure. When the slough separates it leaves a large ulcer, which has already been described. Many believe decubitus to be an example of neuropathic gangrene, as it occurs so readily after injuries to the spine. The rapidity with which sloughs form on the heels after such injuries is certainly suggestive of trophic changes. There is no direct proof of this theory, however, and the general opinion appears to be that the gangrene is due to enfeebled circulation with uninterrupted pressure. Continued pressure, even when too light to cause pain, as from a tightly-applied tourniquet or from splints, produces the same effect. Bed-sores form readily in patients affected with low forms of fever, and they are in such cases partly due to enfeebled heart-action.

In the *treatment* of decubitus great care should be taken to prevent pressure on the parts liable to be affected, such as the heels and the sacrum. The skin should be kept clean and dry, and one of the chief advantages of a trained nurse in such cases is the care given to the condition of the integuments of the back. Daily friction with alcohol, keeping the parts dry with toilet-powder, and the use of ring pads to remove pressure are the principal means of prevention. Since the days of trained nurses bed-sores have greatly diminished in number, and their development is a source of much less anxiety to the attending physician. The same cannot be said, unfortunately, of the use of hot-water bottles. It has been the writer's lot to see, as the result of their careless use, extensive sloughs form upon patients while still under the influence of ether. It is a good rule not to allow any hot-water bottles in the bed of a patient coming out of ether: the bed can be heated sufficiently before he is placed in it.

A rare form of gangrene, but one which is nevertheless occasionally seen at the present time, is that known as *symmetrical gangrene* or Raynaud's disease. It is a variety of dry gangrene characterized by two prominent features—the absence of any anatomical lesions of the blood-vessels, and the symmetrical development of the disease in the two halves of the body. It may be found in both an upper and a lower extremity, or in all four extremities, and occasionally the ear, the cheeks, and the nose are affected. Mills reports a case in which the tip of the tongue was slightly affected. A somewhat similar condition is that popularly known as "dead finger," which comes on after exposure to cold, and which is not unfrequently seen in young ladies after a cold bath. The affected finger is distinctly paler than the others and is cold; the circulation, however, soon returns. In the condition associated with symmetrical gangrene the disturbance of the circulation is more profound, and there occurs what the French call "local asphyxia." The pallor is succeeded by a cyanotic color of varying degrees of intensity. On pressure the color disappears, and returns very slowly, showing great feebleness in the circulation. When in this condition the ends of the fingers, the parts most frequently affected, are often quite painful. The color later becomes almost black, and minute blisters appear on the tips of the fingers. The blisters become filled with a sero-purulent fluid, break, and leave excoriations which may remain several days. The color now begins to return, the excoriations heal, and a little conical tubercle is left just beneath the edge of the nail. The improvement is, however, only temporary; the same changes recur, and may be repeated during a period lasting one or two years. In an advanced stage the ends of the fingers are covered with a number of little white scars, the skin being indurated, and they have a thin, sharp, withered look, as if they had been pinched in a vise and had preserved the shape thus given to them. When the vascular disturbance reaches that point which is sufficient to cause death of the part, the transparent cyanotic pulp of the finger has at its central part a small black mass of tissue which subsequently separates as a slough.

No cardiac disease is found in cases of symmetrical gangrene, and the general condition of the patient gives evidence of no form of organic disease anywhere. The vaso-motor disturbance remains at its height for about ten days, and convalescence is established at the end of from three weeks to several months. Occasionally, after one or two attacks, the condition becomes more or less permanent, and the part affected is continually cold and torpid. At times the skin of the backs of the hands and the fingers becomes thickened and rigid, and the fingers are held semiflexed and ankylosed.

The two affections most likely to be mistaken for this disease are chilblains and senile gangrene. In chilblains all the extremities are not likely to be found affected, and the disease is limited to certain periods of the year. Senile gangrene is rarely bilateral: it is much more extensive, and the characteristic condition of the arteries is usually present. Owing to the predominance of pain it has sometimes been mistaken for gout. The prognosis of symmetrical gangrene is favorable. If the stage of gangrene develops itself at the end of a week or ten days, it is probable that a complete recovery will follow the separation of the eschars. If, however, the disease does not reach this point, but comes and goes, there is danger that it will settle down into a chronic condition. In four-fifths of the cases the disease is found in women. In the great majority of cases it occurs between the ages of eighteen and thirty years. As a low temperature is an exciting cause, the disease is more frequently found on the approach of the winter months. Not infrequently there may be premonitory symptoms for one or two winters, with return to health in the summer season, and a final termination in gangrene.

The following case is the only example of this affection which the writer has seen:

A rather feeble woman, twenty-five years of age and a native of Scotland, presented herself at the hospital in June, 1878. She had been in good health until four months previously, at which time she suffered frequently from nose-bleed. Soon after this she noticed that the tips of the fingers and toes became red. At the time of entrance to the hospital the pulps of the fingers and toes were discolored. The borders of the affected area resembled the semi-transparent purple of a grape. There was none of the reddish tint seen in strangulated intestine. The lightest shades were also essentially purple in tint: near the centre the hue deepened until it was difficult to determine whether or not the tissues were gangrenous. The patient did not complain of much pain, but was totally incapacitated for work, owing to the condition of her hands. On two of the finger-tips were patches of gangrene. In a few days several sloughs separated from the fingers as dry, black eschars, the largest being about the size of a ten-cent piece. The treatment consisted in administration of iron internally and good food, and the application of resin cerate to the parts. About two months later, when the patient left the hospital, the fingers had healed and presented a red and shrivelled look. There was no gangrene of the toes.

Symmetrical gangrene, according to Raynaud, is a form of ischæmia due to contraction of the arterioles, which contraction may sometimes extend back as far as arteries of considerable size (radial pulse). In the lighter forms of spasm there occurs "local syncope" or "dead finger." The veins probably are also contracted. When the reaction following the spasm is incomplete there is "local asphyxia." The veins having the smallest amount of muscular fibres relax first, and the venous blood flows back into the capillaries, but stops here, as the arteries are still contracted. As a result of this condition there is a certain amount of stagnation in the larger veins, and sometimes slight œdema. The arterial contraction was demonstrated in the retina in a case where there was disturbance of vision during the attacks. It is evident, therefore, that the disturbance lies in the vaso-motor apparatus. The symmetrical character of the lesion is explained by an irritation of one of the vaso-motor centres of the cord which brings about a spasm of the vaso-constrictors.

As the disease is situated in various parts of the body, the centre of irritation is not always at the same point, and as there exist several vaso-motor centres, different points may become the seat of the contractions. The vaso-motor nerves are affected not only by direct irritation, but may also be susceptible to reflex action. An example of the latter is the contraction of the vessels of one hand when the other hand is suddenly plunged into very cold water.

Inasmuch as symmetrical gangrene follows occasionally the puerperal state or may show itself periodically at the menstrual epoch, it is but reasonable to suppose that the reflex irritation may take its origin in the uterus. Some of the cases described by Mitchell as *erythromelalgia* have a resemblance to this affection, and some of them undoubtedly appear to be symmetrical congestions. Although this arterial spasm shows itself at the most peripheral portions of the body, it probably is to be found elsewhere, but the parts being less exposed to the loss of heat, gangrene does not occur.

The treatment of symmetrical gangrene consists principally in the administration of tonics and in placing the patient under the best hygienic conditions. Raynaud recommends the use of constant descending currents to the spine. The use of some local stimulating application may serve to restore the tone of the circulation of the part after the arterial constrictions have ceased. During the separation of the sloughs a careful antisepsis of the part should be maintained.

The action of chemical agents as the cause of gangrene has been noted. There is one drug (now so universally used as an antiseptic agent) which occasionally exerts such a powerful local action that it is desirable for the writer to warn against its use under certain conditions. Watery solutions of carbolic acid when applied to the fingers on compresses have in a number of cases been followed by gangrene of the entire finger. Several such cases have come to the writer's knowledge. Strong solutions of this acid have a numbing influence upon the part, and, in the early days of its use, strong carbolic acid was experimented with as a local anæsthetic for minor operations. A prolonged application of a compress wet in a carbolic solution is followed by the evaporation of the water and a corresponding concentration of the agent. The surgeon should therefore avoid entirely the use of solutions of this drug on the extremities of the body. The danger of "*carbolic gangrene*" is one that should always be kept in mind.

Ainhum (a native word meaning to *saw off*) is an affection which occasionally terminates in gangrene, although spontaneous amputation of the part affected may occur without gangrene. It is a disease characterized by a constriction of the integument of the little toe at its plantar fold, producing a deep fissure which gradually encircles the toe until the latter is attached to the foot by a narrow pedicle. Ainhum, which occurs almost exclusively in negroes, is found in Africa and the West Indies; it has also been met with among the Hindus. It is seen more frequently in men than in women. Cases are reported in which the finger was affected, but they are rare. It is said to be hereditary.

There is apparently little if any ulceration during the constricting process. Ainhum has been compared to scleroderma, and Eyles describes a thickening of the deeper layers of the cutis vera. According to Duhring, it may be grouped with "degenerative fibromata." The epidermis is much thickened. The bones undergo an osteoporosis or a rarefying ostitis. The condition known as "obliterating endarteritis" has been observed. As the constriction deepens the end of the toe enlarges, and appears as if it had been encircled by an elastic ligature. The disease may last from one to ten years.

A healthy male negro, fifty-three years of age, suffering from this affection, presented himself at the Massachusetts General Hospital. His family resided in the British Provinces. His grandfather, father, brother, and two sisters had all lost the little toe of the left foot. The toes of all had been removed by a surgeon, except that of one sister, who pulled off her toe.

In the case of the patient the disease began four years before in the same toe. There had been no pain, although sensation was felt in the affected part. The disease when first seen resembled a soft corn, in which a deep furrow existed. The furrow gradually increased until the toe was only attached by a pedicle about one-eighth of an inch in diameter. There was a slight excoriation at one point, but no distinct ulceration, the toe being much enlarged. On removal the toe was placed in alcohol, and after hardening was divided by a horizontal incision, the knife easily cutting through the bone. The phalanx had almost entirely disappeared, and the bulk of the tissue appeared to be made up of a mass of adipose tissue. The cutis and epidermal layers did not appear to be hypertrophied. The patient made a good recovery.

No cause has yet been assigned for this affection. It has been suggested that the constriction has intentionally been produced by a ligature. Possibly it may be due to mechanical friction, owing to some peculiarity in gait or in footgear. Sudan noticed in several cases that lumbar pains preceded the local affection, and he does not regard the disease as local in origin. It has been suggested that division of the constricting bands of fibres at an early stage of the disease might check its progress. In the majority of reported cases amputation was performed. This can be done usually with a pair of scissors, as the bone has disappeared from the pedicle.

XI. SHOCK.

"ALTHOUGH the fact of death ensuing upon injuries of parts not essential to life, even when unattended by hemorrhage, and upon operations not usually esteemed hazardous, has not escaped observation, writers and teachers seem to have contented themselves with the bare statement of it, either from an impression that, being an equivalent in effect to death on the spot or being due to an idiosyncrasy moral or physical, the further consideration of the subject in a practical view was unavailing." Thus writes Travers, the senior surgeon of St. Thomas's Hospital, in 1826. Previous to this time the term "shock," as now used, had rarely been employed as a surgical expression. Guthrie, however, speaks of the "shock of the injury," and Sir Astley Cooper says in his lectures, "The most severe injuries by shock to the nervous system cause death without reaction." James Latta, in 1795, is said to have been the first to have used the word to describe this condition.

This profound but somewhat obscure disturbance of the system, although probably recognized by the practical surgeon from time immemorial, has only received the somewhat tardy attention of medical writers, and even at the present time its pathology is but very imperfectly understood. At all events, the most diverse views have been held by those who have studied the condition of the system in shock. Its importance was first recognized by English writers, to whose efforts no doubt much of our present knowledge is due. Travers, Jordan, Savory, and many others have given the subject special study. It seems strange that the progressive Germans should have allowed shock to have passed almost unnoticed until 1867, when Billroth and Neudörfer first called attention to it.

The nomenclature of the affection is not a large one. The terms "traumatic torpor" and "stupor" have been used by Pirogoff; "prostration without reaction" is spoken of by Travers; Savory uses "collapse" as the title to his article; and "neuroparalysis" has been employed by those who have attempted to explain the nature of shock in this way. In Germany *Wundschreck* and *Erschütterung* are terms that have been used to a limited extent, but they have given way, as in France, to the very expressive English phrase which is now almost universally employed.

Though the literature of the subject is considerable since it received a place in surgery, yet few writers attempt to define the nature of *shock*. Its pathology is usually passed over briefly, and the term may be said to have been employed indiscriminately to describe all cases of sudden death following injury without hemorrhage. In America and in England the condition has been regarded as a general depression of the nervous system without any very well-defined idea as to what the nature of the change was. Mansell-Moullin has defined it a little more accurately as a reflex paralysis or inhibition of the nervous system. In France, Blum explains shock as an arrest of the heart's action, due to reflex irritation of the pneumogastric nerve. In Germany many writers have adopted the theory of Fischer, who attributes the weakness of the heart's action and the other phenomena of shock to a reflex vaso-motor paralysis whereby the abdominal vessels are hyperæmic, and the heart, brain, and other organs are correspondingly ischæmic.

Before going more deeply into this question let there be a mutual understanding of the *clinical picture* which this subtile condition produces in the human organism, when, as Gross graphically puts it, "the machinery of life has been rudely unhinged."

A patient is brought into the hospital with a compound comminuted fracture or with a dislocation of the hip-joint added to other injuries, where the bleeding has been slight. As the litter is gently deposited on the floor he makes no effort to move or look about him. He lies staring at the surgeon with an expression of complete indifference as to his condition. There is no movement of the muscles of the face; the eyes, which are deeply sunken in their sockets, have a weird, uncanny look. The features are pinched and the face shrunken. A cold, clammy sweat exudes from the pores of the skin, which has an appearance of profound anæmia. The lips are bloodless and the fingers and nails are blue. The pulse is almost imperceptible; a weak, thread-like stream may, however, be detected in the radial artery. The thermometer, placed in the rectum (it would be useless to attempt to take the temperature in the axilla), registers 96° or 97° F. The muscles are not paralyzed anywhere, but the patient seems disinclined to make any muscular effort. Even respiratory movements seem for the time to be reduced to a minimum. Occasionally the patient may feebly throw about one of his limbs and give vent to a hoarse, weak groan.

There is no insensibility (coma is not observed in cases of shock), but he is strangely apathetic, and seems to realize but imperfectly the full meaning of the questions put to him. It is of no use to attempt an operation until appropriate remedies have brought about a reaction. The pulse, however, does not respond; it grows feebler, and finally disappears, and "this momentary pause in the act of death" is soon followed by the grim reality. A post-mortem examination reveals no visible changes in the internal organs.

The two principal theories as to the *nature* of shock are based on certain functional disturbances in the vascular and nervous systems respectively. Fischer takes the ground that shock produces a paralyzing effect upon the heart in a manner similar to that produced upon the frog in Goltz's experiment, which consists in the infliction of repeated slight blows upon the abdomen (p. 85). When the heart begins to pulsate again it remains small and pale, and receives in the diastole very little blood, and is therefore able to throw out only a small quantity into the system. This condition was ascribed by Goltz to a lack of tonicity in the vessels of the abdominal cavity, but later he was convinced that there was a very general vaso-motor paralysis. It was shown also that the same condition could be brought about by blows received in other parts of the body. This lack of tonicity Goltz subsequently showed was not confined to the arteries, but might affect the veins also, and in this way such large quantities of blood might be received in the vessels of the abdominal cavity, as has been shown experimentally to be the case after division of the splanchnic nerves, that the heart and large vessels elsewhere could receive but an extremely small quantity of blood. According to Fischer, then, the great mass of the blood stagnates in the abdominal veins and arteries during shock. This, he thinks, is a sufficient physiological explanation of the symptoms of shock. As the skin is anæmic, it is pale, cold, and without sensation. Experiment has shown that muscles deprived of their blood are rigid and unable to perform their functions, and the great muscular weakness is therefore accounted for. The irregularity and the temporary cessation of the heart's action account for the small, irregular, and absent pulse. The cerebral anæmia explains the mental phenomena of shock and the nausea and vomiting.

Schneider also adopts the theory of a reflex paralysis of the vaso-motor nerves, as based upon the views of Falk and Sonnenburg on the cause of death after extensive burns. According to Schneider, every extreme irritation produced by surgical operations or by injuries causes at first contraction, and subsequently general dilatation, of the blood-vessels. "The heart is unable to force the small amount of blood through the empty vessels. Its own muscles are insufficiently supplied with oxygen, and it gradually ceases to beat. The great lowering of the temperature of the body can be explained by the diminished blood-pressure, and consequently the increased difficulty in providing oxygen for the tissues, or by the retarded flow of blood and the consequent increase of the loss of heat, or finally by the direct influence upon the heat-centre." Thus the theory of Fischer is extended so as to include a vaso-motor paralysis of the whole vascular system. This view is accepted by Mansell-Moullin, who considers it an enormous advance on all previous views, but still cannot accept it as thoroughly sufficient to explain all the phenomena of shock. He assumes these vaso-motor changes to be produced by inhibition, rather than by simple reflex paralysis, and, arguing on this basis, suggests that the same power may be the direct and immediate agent influencing the nerves that govern sensation, motion, and volition as much as those that control the walls of the blood-vessels. The molecular action which constitutes nerve-force may be interfered with, perhaps even interrupted, not only in certain centres that control the heart and vascular system, but also in other centres. "Shock is to be regarded as an extreme and general manifestation of that inhibition with the power of which, as regards a few organs, physiology has made us acquainted." "In short," he concludes, "shock is an example of reflex paralysis in the strictest and narrowest sense of the term—a reflex inhibition, probably in the majority of cases general, affecting all the functions of the nervous system and not limited to the heart and vessels only."

The vaso-motor theory is also held by Gross, for he states that shock is essentially dependent upon reflex paralysis of the entire circulatory system, but especially of the heart and abdominal vessels. It has gained numerous adherents in Germany, among whom may be mentioned Eulenburg and Schede.

Grœningen, however, takes exception to the vaso-motor-paralysis theory, and shows that Goltz himself did not regard this as shock, but rather as syncope or "fainting." Many of the symptoms of shock can, he acknowledges, be explained by this theory, particularly those belonging to the circulation—not those, however, connected with motion and sensation. The anæsthesia and paresis produced in the posterior extremities of a rabbit after ligature of the abdominal aorta do not correspond to those symptoms produced by shock. The return of blood to a part thus rendered anæmic is usually exceedingly painful, and there are also peculiar creeping sensations. No anæsthesia is produced by the Esmarch bandage. In shock there is no sensation whatever in the muscles. Anæmia of the brain is one of the symptoms of syncope, not of shock. If Fischer's theory were correct, the signs of shock and hemorrhage would be the same, but, as will be seen later, there are important differences in this respect. In rabbits subjected to the Goltz experiment Grœningen was unable to demonstrate an anæmia in the peripheral arteries and muscles. In rabbits dying from shock he found the abdominal arteries and veins empty. All possibility of hyperæmia of these vessels may be removed by administering Calabar bean to these animals, and yet the symptoms of shock may be produced. Many claim that in the mammalia sufficient blood cannot be made to collect in the abdominal vessels to produce this so-called "intravascular hemorrhage." Division of the splanchnic nerves in animals does not produce the symptoms of shock. Cases of sudden abdominal plethora following premature delivery, or of sudden emptying of effusion from the abdominal cavity, are incorrectly called "shock," according to Grœningen, being in reality brain-anæmia.

In addition to these arguments, there may be adduced the practical experience of those surgeons who are accustomed to operations in the abdominal cavity. It has certainly been the writer's experience that the symptoms of shock are not accompanied by any marked change in the blood-supply to the abdominal vessels. A careful analysis of this theory shows, therefore, conclusively, that it does not account satisfactorily for all the symptoms of shock.

Many surgeons regard shock as a sort of heart failure, a temporary paresis of the muscles of the heart. Savory, whose article has long been an established authority on shock, says: "The heart is powerfully affected through the nervous system, and its action is arrested." Blum has endeavored to explain the functional disturbance of the heart in shock by the action of the pneumogastric nerve similar to that caused by experimental irritation of the nerve, which produces either a diminution in the number of beats or a sudden interruption of the heart's movements. This explanation would not account for those cases of shock in which the rapidity of the heart's action is increased. Irritation of this nerve does not always produce the same changes in blood-pressure, whereas in shock there is always a general and considerable diminution in the blood-pressure. This theory, moreover, does not explain the weakness of muscular action and the diminished sensitiveness and many other symptoms of shock. In cases of irritation of the pneumogastric nerve produced in man by pressure upon the carotid region the number of pulse-beats per minute is diminished one-half, but the beats continue to be strong, as does also the action of the heart. The arterial pressure was temporarily diminished, but afterward was above normal.

Grœningen observed the case of a hussar who was kicked on the left side of the neck by a horse. In addition to a paralysis of the left vocal cord, there was, for several days, a remarkable reduction of the heart-beats to thirty per minute. The pulse was, however, strong and the heart's action good, although slightly irregular. Meyer found that by electric stimulation the heart's action could be arrested for a minute in warm-blooded animals, but he was unable to produce any permanent impression upon the motor apparatus of the heart. Finally, post-mortem examinations show that irritation of the pneumogastric causes arrest of the heart in diastole. In cases of death from shock the heart is often found contracted and empty. It need hardly be added that paralysis of the heart produced by irritation of the pneumogastric nerve cannot be accepted as the cause of shock on such evidence.

Many of those authors who have been inclined to accept the vaso-motor theory of shock have nevertheless not been fully satisfied with its capacity to account for all the symptoms. Mansell-Moullin's opinion on this point has already been quoted. The same view is held by Mitchell, who says: "Either the shock of a wound causes paralysis of vaso-motor nerves and sequent congestion, with secondary alterations, or it destroys directly the vital powers of a centre. Now, there is no reason why if shock be competent to destroy vitality in vaso-motor centres or nerves, it should be incompetent to so affect the centres of motion and sensation."

Cooper was clearly of the opinion that death in some injuries was caused by both direct and indirect shock to the nervous system. Billroth undertook to explain the change thus produced as a molecular disturbance of certain portions of the brain. Brown-Séquard recognizes an irritation of the cervical cord, the medulla, and the neighboring central structures as shown by the effect upon the vagus, the sympathetic, and sensitive nerves. There is, he thinks, a weakening also of the nerve-power at the respiratory centre.

One of the most thorough and complete studies of the action of the nervous system in shock has been made by Grœningen. An indication of this action is given by Leyden, who ascribes the phenomena of shock to a powerful irritation either directly upon the cord or indirectly through a peripheral sensitive nerve, by which a profound molecular disturbance is produced in the nerve-tissue, which is thereby incapacitated from receiving less intense stimuli. The functions of the cord may thus be paralyzed or be reduced to a minimum. Among these functions there must be included not only sensation and motion, but also those which preside over the heart, the vaso-motor nerves, and the respiration. "The brain," he says, "does not participate, the mind is clear: it is rare that stupor, coma, or delirium is present."

Let us see for a moment what the result is of the functional activity of the nerve when subjected to a mechanical irritation. If a sensitive nerve is irritated, a change takes place in its equilibrium which is transmitted peripherally and centripetally. As to the centrifugal change nothing is known. The centripetal irritation brings about a change which is called "sensation." In the nerve as well as in the nerve-centre there is a certain amount of consumption of tissue, perhaps also a molecular change. In fact, it is known that after repeated irritation there is a chemical change in the nerve, and that its power of responding to further irritation is diminished. The mere act of function, therefore, brings about a change which is called "fatigue," and, when extreme in degree, "exhaustion." The fatigue disappears after a certain interval with rest, and the nerve resumes its former power of responding to irritation. In the case of the motor nerve the irritation expresses itself centrifugally in muscular action. Here also both nerve and muscle may become exhausted by repeated irritation.

As Savory puts it, "Action involves exhaustion, and repose is needed for repair. The greater the effort, therefore, the greater the exhaustion." The exhaustion of the *peripheral nerve* depends partly upon the degree of the irritation, and partly also upon the suddenness with which it is exerted. It follows, therefore, that a single sudden maximum irritation produces the highest degree of exhaustion. Experiment shows that the irritation is not confined to the nerve alone, but spreads from its point of origin to certain portions of the central nervous system.

So far as the *amount of the irritation* goes, Grœningen recognizes four degrees: (1) The lowest is without perceptible action on the nerve; (2) the second disposes of the sense of feeling, such as touch, sight, hearing, taste, and smell; (3) a stronger irritation effaces more or less the acuteness of these perceptions, and brings out prominently the sensation of pain or of such disagreeable sensations as loathing, disgust, etc.; and (4) the highest degree of irritation destroys all sensation either temporarily or permanently.

Each lower degree of irritation leads insensibly up to a higher one. The sensation of heat and cold may merge into that of pain. So with the other senses: a strong light may blind, an intensely loud noise may cause deafness. Again, a higher degree of irritation prevents the perception of one of lower grade: the lips are bitten to suppress the pain of an operation. A maximum of irritation may be reached when all special senses are destroyed, and even pain itself is not felt. With all these changes of function the nerve remains anatomically the same, to all appearance. The paralyzed nerve and the nerve afflicted with the most intense neuralgia may have no marks to distinguish one from the other. The disturbances recorded are therefore considered purely functional.

Let us now look at the *nerve-centres*. The change in them produced by irritation is usually called "reflex inhibition," but the phenomena thus produced can as readily be explained by the theory of fatigue of these centres caused by over-irritation. Reflex paralysis is an example of fatigue of the nerve-centres. Lewisson showed that if the kidney of an animal was seized and squeezed by the hand, a temporary paralysis occurred in the posterior extremities and reflex irritability was for the time destroyed. Mitchell reports numerous cases of reflex paralysis following injuries to nerves. Here exists paralysis of the motor apparatus as the result of irritation of a sensitive nerve. These paralyses were in remote regions and unconnected with the injured limb, and they appeared after the first shock of the injury had subsided. Langenbuch showed that after nerve-stretching the pulse was smaller and more frequent or slower, the breathing more superficial or changed in rapidity.

From these examples it is seen that during the simple process of innervation the nerve-centres may become fatigued to a greater or lesser extent, and that when the irritation of the peripheral nerves is very intense the functions of those portions of the cord receiving or transmitting these impressions may be temporarily interrupted. *A condition of fatigue or exhaustion* is thus produced that shows itself in a weakening or suspension of the sensitive and motor functions of these portions of the cord.

The changes which are due to exhaustion must not be confounded with inhibition. The reflex centres are a portion only of those that are affected. The motor centres are also paralyzed, sensation is weakened, the perception of pain is benumbed, the temperature falls, respiration is less active, the vaso-motor centres are enfeebled, and the strength of the heart fails. As Grœningen says, the spinal cord up to its point of origin from the brain is suddenly overwhelmed, as it were, and can only regain its vitality after a complete rest.

It has hitherto been supposed that the nature of this *condition of the cells of the cord* was not demonstrable by any method of examination, and the change which takes place was therefore regarded as molecular, such as one might expect to find in a purely functional disturbance. The observations of Hodge, however, are very suggestive in this connection. This observer has made a microscopical study of changes due to functional activity in nerve-cells, hoping to find alterations corresponding to those seen in the cells of a gland which is performing its functions. The gland-cell during rest becomes filled with granules, and during secretion these granules pass out, generally leaving the cell shrunken. "The necessity for rest in a gland-cell is made apparent by its loss of substance. If nerve-cells do not lose substance or change in some way, why are we tired at night?" To test this question Hodge subjected the spinal ganglia of frogs and cats to electric stimulation for several hours, comparing the changes observed in the cells with the normal cells and with stimulated cells after a period of rest. He also studied the effects of normal daily fatigue in sparrows, swallows, and bees. The ganglia of birds obtained in the early morning were compared with those of birds killed at the close of a hard day's work. He concludes that metabolic changes are as easy to demonstrate microscopically as similar processes in gland-cells. These alterations consist in a marked decrease in the size of the nucleus, and a change from a smooth and rounded to a jagged, irregular outline. There is a loss of the open reticulate appearance of the nucleus, and it takes a darker stain. There is a slight shrinkage in size with vacuolation in the cells of the spinal ganglia, and considerable shrinkage with enlargement of pericellular lymph-space for cells of the cerebrum and cerebellum. The protoplasm does not take the staining material so well as when in its normal condition. There is a decrease in the size of the nuclei of the cell-capsule when present (Fig. 64).

These interesting results seem to throw new light upon the condition of the ganglia of the cord and medulla in the condition known as shock, and render the supposition highly probable that in this profound functional disturbance similar changes may be found which may gradually disappear after an interval of rest.

Some writers undertake to distinguish several *varieties* of shock. That variety of which a brief clinical picture has already been given is the most frequent, and is called by some the "torpid form of

FIG. 64.—Ganglion-cells from the Cord of a Cat: *a*, cell stimulated seven hours; *b*, resting cell.

shock." Travers in his account of shock uses the term "prostration with excitement," which was intended to describe a particular form of shock. About this variety, which has frequently been mentioned by subsequent writers, there has been much discussion. Mansell-Moullin thus describes it: "The patient tosses wildly and vaguely from side to side as if frantic, complaining of a fearful oppression and want of breath, with presentiments of death and a feeling of total annihilation; often shouting again and again the same thing. . . . . No encouragement is of any use: the consciousness is unclouded," etc. Cheever thus concisely defines this condition: "Typhoidal delirium, a dusky flush over the malar bones, dull eyes, intermittent pulse, jactitations, exhaustion, death." Travers in his account of this condition quotes two illustrative cases, one of which appears to be an attack of acute mania following injury to a person who had previously been insane. The other, a rapidly-fatal case, closely resembles one of fat-embolism.

In severe hemorrhage there is a peculiar restlessness which might show itself notwithstanding the accompanying shock, but hardly to such an extent as in this form of shock. There are, however, cases where little or no bleeding has occurred when after an injury there is immediately great excitement. Mitchell has described graphically several such cases in his article on "Injuries of the Nerves." In one case of gunshot wound of the right wrist-joint, injuring the ulnar and median nerves and causing cerebral excitement, the patient, who was a colonel, ran along the line of his regiment "half crazed," in a state of wild excitement, and presently fell insensible, but not from loss of blood. In another case of shot-injury to the right median nerve the patient, also an officer, was helped to the rear, talking somewhat incoherently about matters foreign to the time and scene. He was very feeble, but lost little blood, and he had not the least remembrance of having been shot or of any event which followed an hour afterward.

Grœningen, although inclined not to accept this form of shock, suggests that it may be one following a condition of exaltation occurring after injury, and Roberts, speaking of delayed shocks, says: "Another explanation I venture to offer for some of those cases is the reactionary mental exhaustion that may occur after mental excitement and simulate shock." It is probable that some of these cases may be ascribed to that condition known as "delirium nervosum" or "delirium traumaticum."

The so-called *secondary* or *delayed shock* may be due to secondary complications; it is probable that the term originated at a period when the pathology of fat-embolism or septic infection was less understood. In certain cases of shock the patient may sometimes linger for one or two days before finally succumbing to exhaustion, and in this sense there may be such a condition, but it is usually called "protracted shock," and is hardly to be classed as a separate variety.

Gross describes a variety known as *insidious shock*, which the writer thinks many surgeons will recognize as characteristic of true shock. The symptoms are of a marked character, however, and well calculated to deceive both patient and practitioner. "The person, though seriously injured, congratulates himself upon having made an excellent escape, and imagines that he is not only in no danger, but will soon be about again. . . . . The countenance in this form of shock has often a peculiarly melancholy expression, as if foreshadowing the fatal event; a sad smile plays upon the lips and illumines the lower part of the face, while the upper part wears a gloomy aspect in striking contrast with the other." It seems to the writer that in such cases there had been an attempt at reaction which had failed. The cheek may be flushed slightly and the skin be dry and warm; but the pulse, although stronger, is easily compressed, and it is evident to the careful observer that the patient's condition is most critical. He may greet you with a cheerful "Good-morning, doctor," and when asked how he feels will respond, "Fine;" and yet the fatal end may come only a few hours later.

Several writers speak of *local shock*. Pirogoff mentions "la stupeur locale." Grœningen defines it as peripheral shock. It should not be confounded with the bruised and benumbed fragments of tissue in the immediate neighborhood of a wound. It seems to consist in diminution of sensation and of motion in the adjoining apparently healthy tissues, which is probably of central rather than of local origin. Gussenbauer claims to have seen this condition even when the symptoms of general shock have been very slight. It is analogous to some of the *reflex paralyses* so often observed, but in this case it is near rather than remote from the wound. Berger has noted in some cases a complete hemi-anæsthesia involving not only the skin, but the adjacent mucous membranes. This anæsthetic condition is in some cases so marked that operations have been performed without pain. Many acts of heroism of this nature on the battlefield are mentioned by surgical writers.

Among the most frequent *causes* of shock are the severe injuries which surgeons are accustomed to see in hospital practice. Among these injuries are the compound comminuted fractures of the bones of the extremities that are so frequent among railroad employés or machinists. Penetrating injuries involving the viscera are nearly always accompanied by considerable shock, though this primary condition must not be confounded with the septic disturbance which often follows with great rapidity. Injuries of certain organs, as of the testicle and bone, are supposed to produce shock more readily than in other parts. A blow on, or the crushing of, the testicle may produce a certain amount of shock. Bristowe reports a case of severe shock following a blow by a shot which grazed the testicle. Hunter mentions a sudden death during castration. Fischer reports the case of a fine healthy man who was attacked by an enraged horse. The testicle was seized by the animal, and the scrotum was held for a considerable time between the animal's teeth and severely lacerated. The man died in a few hours from shock.

Operations upon the testicle, as conducted at the present time, are rarely followed by the symptoms of shock. Operations upon the urethra, such as catheterism, are often followed by syncope, but it is not in accord with the writer's experience that genuine shock can be produced by this cause. The very extensive operations which are now performed for necrosis do not seem to be followed by shock more frequently than any other operations of the same magnitude. All capital operations, particularly those prolonged over a considerable period of time, produce shock. Primary amputations at the hip-joint were almost invariably fatal during the War of the Rebellion. The method then employed involved serious hemorrhage, which always greatly aggravates the condition of collapse due partly to the injury and partly to the operation. This operation was finally prohibited by the surgeon-general.

According to Billroth, the evulsion of an arm or a leg is usually followed by a fatal shock. Fischer, however, relates the case of a lion-tamer whose whole left arm was torn from the shoulder-joint by a lion. The loss of blood was very slight, and the patient was so little affected by shock that he was able to walk to the hospital. Loss of blood is a powerful factor in the production of shock, and many of those cases which have terminated fatally may have been largely due to hemorrhage. The present "completed" operation for removal of cancerous breasts is likely to be followed by serious shock if this detail be not attended to. "The more sudden the loss of blood, the greater will be the immediate prostration and the less are the chances of recovery" (Gay).

Blows upon the chest are usually not followed by much shock, which is of short duration, and which is due as much to the general effects of the injury as to the local lesion. "The pit of the stomach" or the abdomen is a much more sensitive region. Examples of shock from this form of injury are innumerable. Vincent relates the following case: "A man received a blow from a stick upon the epigastrium. He had an anxious expression and suffered from oppression, irregular heart-action, and shivering, symptoms which gradually disappeared during the day. In the evening his appetite returned, and he felt well: during the night he died without a struggle. At the autopsy there was absolutely nothing abnormal to be found."

Blows received during football or baseball matches have terminated fatally with the same symptoms. Such cases remind one of the frog experiments of Goltz, and of Fischer's vaso-motor theory of shock. Doubtless many of these cases may be shown to owe their fatal termination to a weak heart. Grœningen attributes the shock in such cases to the peculiar anatomical distribution of the nerves to the abdominal viscera. Here are found the rich plexuses of the sympathetic system with the large ganglionic masses, most prominent among which is the semilunar ganglion, named by Bichat "le cerveau abdominal." A very powerful irritation may suddenly be transmitted to the cord and the medulla oblongata, and the subsequent exhaustion of the vital nerve-centres may thus be produced. The writer is inclined to think, however, that a certain number of these cases may be due to the vaso-motor disturbance produced by a temporary paralysis of the splanchnic nerves. This theory seems at least more closely in accord with physiological experiments. Such cases, therefore, should not be regarded as cases of true shock.

Blows upon the neck often produce sudden collapse. There has already been alluded to the effect of a blow upon the pneumogastric nerve and the symptoms thus produced. In those cases under consideration, however, the patient drops vertically to the ground in an unconscious condition. Prize-fighters are well aware of the opportunity which a blow "upon the jugular" offers to save themselves, perhaps, from a threatening defeat. Various theories have been offered to explain the nature of this injury. To some pathologists it is known as *concussion of the larynx*. Fischer assumed that spasm of the glottis was thus produced. By Claude Bernard and others it is supposed that an inhibitory action is exerted upon the respiratory centre through an irritation of the superior laryngeal nerve. It is known that swimmer's cramp is produced by some such powerful stimulus sent to the respiratory centre, and it is probable that the sudden unconsciousness caused by garotting is produced in the same way. A blow in this region would also bruise the cervical sympathetic plexus of nerves, and it is possible that a sudden cerebral anæmia could thus be produced. It seems to the writer that many of these cases should be interpreted in this way and be removed from the category of shock. That true shock may, however, be thus produced seems apparent from cases reported by Maschka, of which the following is an example: A boy, twelve years of age, received a blow from a stone upon the anterior portion of the larynx. He fell lifeless to the ground. At the autopsy no local lesion was found and no injury elsewhere. The sudden death may be attributed in this case, in part, to shock and in part to cerebral anæmia.

In severe burns which have affected more than one-third the surface of the body the symptoms of shock are always well marked. It has been suggested that extensive dilatation of the blood-vessels upon the surface of the body causes diminution of blood-pressure, and that the heart's action is thus weakened. Billroth attributes the symptoms to shock produced by the severe irritation of the nerve-centres through the peripheral nerves, and it is probable tha the condition of such individuals is one of true shock. Similar results, according to Gay, may be produced by swallowing irritating poisons, as oxalic acid or corrosive sublimate. The constitutional effects of such poisons as prussic acid or nicotine or the poison of serpents should be regarded as collapse due to the action of the poisons rather than to true shock. Sudden death from lightning is also due to shock. Grœningen reports the case of a soldier who recovered from lightning-stroke in whom the symptoms of shock were well pronounced.

Cases of sudden death often follow the tapping of cysts, particularly in the abdominal cavity. Many of these cases should be regarded as local hyperæmias due to the sudden removal of pressure from the abdominal blood-vessels. In some cases when the aspirator has been used air has unintentionally been forced into the veins and an embolism thus produced. Moullin reports a case of death in five minutes after tapping the liver for hydatid disease. The only sign of organic disease found at the autopsy was a slightly granular condition of the kidneys.

The sensitiveness of the abdominal cavity has already been mentioned. In abdominal operations shock may be produced and be aggravated by prolonged handling of the intestines and the breaking up of extensive adhesions, and the exposure of the viscera to the air, whereby a great amount of heat is rapidly lost. Great shock is caused by a rupture of the viscera, particularly of the intestines. In strangulated hernia the symptoms of shock are often present in a marked degree. Even after the constriction has been relieved fatal shock may supervene. This peculiar condition has been recognized by French writers under the name of *peritonisme* or *cholera herniare*. According to Mansell-Moullin, the strangulation of a portion of the small intestine, whether in a hernial sac or by some band within the abdominal cavity, is attended at once by symptoms of the most complete prostration, and may of itself, if left unreduced, be sufficient to occasion death without the production of peritonitis.

The relation of pain to shock has been noticed by many writers. Before the days of anæsthesia such a case as the following, reported by Sir Astley Cooper, seems to have been a not unusual occurrence:

A brewer's servant, a man of middle age and robust frame, suffered much agony for several days from a thecal abscess occasioned by a splinter of wood penetrating beneath the nail of the thumb: a few seconds after the matter was discharged by a deep incision the man raised himself by a convulsive effort from his bed and instantly expired.

If it is recalled for a moment what has been said about the different degrees of nerve-irritation, it will be found that very powerful nerve-irritation, such as usually produces shock, is painless. The higher degree of irritation destroys function. For this reason wounds received during battle are not painful. Stromeyer states that nothing is so surprising to the novice in military surgery as this absence of pain. "Perfect quiet reigns in the hospital ward the first night after a battle."

That anæsthesia has served to lessen shock after operations is probably due to the fact that the nerve-centres are thus protected to a certain extent from powerful irritations from without, rather than to the mere absence of pain. Le Gros Clark says: "I think the shock of pain is much overestimated: . . . . it is certain that great and almost continued pain is compatible with protracted life." Grœningen maintains that the theory that shock is caused by pain has not been proven.

Mental emotion is accepted by many writers as a cause of shock, but the theory is received with doubt by others. The following case, reported by Lauder Brunton, has been much quoted:

> Many years ago the janitor of a college had rendered himself obnoxious to the students, and they determined to punish him. Accordingly they prepared a block and an axe, which they conveyed to a lonely place, and, having dressed themselves in black, some of them prepared to act as judges and sent others of their company to bring him before them. He affected at first to treat the whole thing as a joke, but was solemnly assured by the students that they meant it in real earnest. He was told to prepare for immediate death. The trembling janitor looked all around in the vain hope of seeing some indication that nothing was really meant, but stern looks met him everywhere. He was blindfolded and made to kneel before the block; the executioner's axe was raised, but instead of the sharp edge a wet towel was brought smartly down on the back of the culprit's neck. The bandage was now removed from his eyes, but, to the astonishment and horror of the students, they found that he was dead.

Such a case may be due to heart failure from fear and excitement. It is generally conceded, however, that all depressing influences, whether moral or physical, contribute to the aggravation of shock. Soldiers exhausted from great fatigue or from starvation or demoralized by defeat succumb much sooner to shock than do their victorious opponents.

The effect of individual temperament is often strikingly shown after severe injuries. Soldiers of the most undaunted courage turn pale and tremble like a leaf after a comparatively trifling accident (Gross). Mitchell reports the case of an officer wounded in the heel who was instantly thrown into a condition of the utmost trepidation. His character for courage was undoubted, and a court of inquiry, for which he asked, cleared him on the surgical evidence.

Railway injuries are supposed to be a prolific source of shock even in cases where there has been no well-defined external or internal injury. This class of cases, formerly regarded as due to concussion of the spine, has been more recently interpreted by Page as a shock to the nervous system in which a condition is eventually arrived at where the seat of the disturbance seems to be centred in the will-power rather than in any lesion of the nervous system. Cases of this kind may or may not at the time of the accident present the symptoms of true shock. "It is a singular fact that cases attended by symptoms of shock immediately after an accident seldom present the symptoms peculiar to 'shock to the nervous system'" (Gay). The subsequent chronic state of the patient should not be confounded with true shock, but is more closely allied to the condition now known as *neurasthenia*.

Age and sex are supposed to have an influence in producing shock, but it is not probable that there is any material difference in this respect. In youth, as in old age, the nerve-centres probably yield more readily to powerful irritations, and this may also be said of persons whose constitutions are enfeebled by alcohol or by disease.

Great precautions should be taken during the performance of capital operations upon very young children as well as upon the aged, and the condition of the heart and kidneys should always be inquired into in all cases before operation. At one time it was supposed that individuals in robust health were not so well prepared to undergo a severe operation like amputation of the hip-joint as those who were already somewhat invalided by disease. In the former class of cases there is usually the history of a severe accident with its attendant shock and hemorrhage. Obviously in the second class of cases the operation would be performed with all the advantages that a previous preparation of the patient could give.

There have already been briefly alluded to the *symptoms* of shock in a typical case. The most striking of these symptoms to the observer is the sickly-white hue of the skin, the thin, pale lips, and the contracted features: the expression of the face is frequently so altered that it is difficult to recognize a friend. The pupils are but slightly altered, but the eyes are sunken in their sockets. The surface of the body is cold everywhere to the touch, the hands are blanched, and the fingers and nails exhibit a bluish color. The sensation of pain is more or less diminished, but a disturbance of the crushed limb will cause the patient to emit a feeble and hoarse cry.

Muscular action is greatly enfeebled, so that voluntary movements are made but seldom. The excito-motor functions in severe shock are gravely impaired. The lids do not close when the conjunctiva is irritated. Deglutition is difficult. The anal sphincter is relaxed, while the urine is retained. "Under such circumstances, especially when the fifth and glosso-pharyngeal nerves fail to excite any response in the nerve-centres, the gravest fears may be entertained that respiration itself will momentarily yield" (Jordan). The inspirations are shallow, but are occasionally accompanied by sighing and convulsive tremors.

There is no coma, but the mental condition is one of more or less sluggishness, due doubtless to the central anæmia. The condition of the pulse varies with the degree of shock. In the milder forms it is frequently slower than normal, but it is more compressible. In the graver forms it is small, fluttering, and at times almost imperceptible. The thread-like pulse is under these circumstances usually more rapid than normal, the heart apparently endeavoring to compensate by frequent action for the feebleness of the current. The strength of the pulse is a most important guide to the surgeon in estimating the severity of the shock. A more accurate gauge of the degree of shock is to be found in the temperature. To determine this point the thermometer should be placed in the rectum, and if a fall of two degrees below the normal point is registered, the amount of shock is sufficient to contraindicate operative interference. Much lower temperatures have been recorded from observations taken by placing the thermometer in the axilla. The secretions are often much diminished or are altered in their character. The urine is scanty; the catamenia may suddenly cease or may appear. Many writers relate instances of suppression of lactation. A woman suddenly threw herself between two soldiers to save the life of her husband. The chemical condition of her milk was so altered immediately after that the child at the breast was poisoned by it. The great amount of cold sweat upon the forehead has been explained by the relaxation of the mouths of the sweat-ducts. Vomiting is regarded by some as the primary sign of reaction. One of the first evidences of this change is the returning color of the face and the strengthening of the heart's action. Formerly it was supposed that the symptoms now recognized as traumatic fever were simply due to the rebound of the system from the condition of shock, and that they were to be expected as a natural sequence. Reaction is, however, in reality, simply a return of the system to its normal condition. The various functions should therefore, in a case which has been treated antiseptically or where no wound was present, reappear in their natural state of activity. The pulse becomes stronger and fuller, the skin dry and warmer, and the respirations are deeper. The mind regains its self-possession, and the temperature returns to the normal standard.

In making the *differential diagnosis* there are many conditions formerly attributed to shock to be considered which now are recognized as due to other causes. It is only in the gravest forms of hemorrhage that the patient's condition is likely to be mistaken for one of shock. The anæmia from loss of blood can readily be distinguished from shock, as it comes on gradually, perhaps, from recurring hemorrhages, and is an affection of a more chronic type. When, however, the patient succumbs to bleeding from some large vessel or in consequence of the laceration of numerous vessels in some extensive wound, his condition very closely resembles that of shock. John Bell has given a vivid picture of such a case: "The face becomes all at once deadly pale, the circle around the eyes is livid, the lips are black, and the extremities are cold. The patient faints, recovers, and faints again, with a low, quivering pulse; he has nausea, and his voice disappears. There is an anxious and incessant tossing of the arms with restlessness, which is the most fatal sign of all. He tosses continually from side to side; his head falls down in the bed; at times he suddenly raises his head, gasping for breath, with inexpressible anxiety; the tossing of the limbs continues; he draws long and convulsive sighs; the pulse flutters and intermits with the breathing more and more, and he expires." The prominent distinctive features of hemorrhage are the anxious expression of the face, the tossing about of the arms, the great restlessness, and the frequent attacks of syncope.

Acute septic poison, particularly that occurring after operations or injuries of the abdominal cavity, presents frequently a group of symptoms which might readily be mistaken for shock. A perforation of the intestine may have taken place, or a gunshot injury of the bowel has permitted the escape of the contents of the intestine into the peritoneal cavity. In a few moments' time the appearance of the individual changes and the symptoms of collapse are well marked.

In fat-embolism there exists another cause of sudden death after injuries. Fluid fat may be taken into the open vessels and be carried by the lymphatics into the circulation. Fractures of bones furnish the most typical example of this complication, as do also ruptures and contusions of the liver and severe contusions of the skin and subcutaneous fat. Acute suppurations in tissues rich in fat may also produce fat-embolism. It is also found in a greater or lesser degree in acute osteomyelitis. The most frequent seat of these emboli are the lungs. After reposing for a brief time in the vessels of the lung, the fat-drops are carried onward and distributed to various organs, such as the heart, capillaries, skin, brain, muscles, and kidneys, whence they finally disappear. It is only when large amounts of fat accumulate in this way in the capillaries of the lung that a fatal result is brought about. The symptoms of this complication, which occurs within twenty-four or forty-eight hours after an injury, are sudden pallor, irregular heart-action, dyspnœa, perhaps hæmoptysis, or convulsions and death. Fat will be found in the urine.

The presence of air in the vessels in small quantities has been shown by experiment not to be injurious, but when a large quantity has been introduced during a surgical operation the heart may be filled with air, and then is unable to contract. Death under such circumstances will be instantaneous, and will be attended with the symptoms of syncope. This extremely rare occurrence can only happen, according to Hare, when a pint or more of air has been introduced at once into the circulation.

Fainting or syncope is regarded by Travers as differing only in degree from shock. It has already been shown that syncope is due to disturbances of circulation only. Preliminary nausea, ringing in the ears, and dizziness, followed by a fainting fit, during which the patient is temporarily unconscious, are symptoms of acute cerebral anæmia, and not of shock. In concussion of the brain there are, according to Fischer, an arterial anæmia and venous stasis. The experiments of Koch and Filene showed no central lesion, and they conclude that the vaso-motor centre is not only affected, but that all other cerebral centres of activity are temporarily exhausted and paralyzed. There is here a condition closely resembling that which in the cord and medulla is called "shock." Some writers, however, point out that there must be some physical change, for the brain is never fully restored to its former condition, as the memory of what has happened immediately before the injury never returns, and in this respect concussion differs from shock in its nature. Duret has, in fact, observed a laceration of the floor of the fourth ventricle, due to the forcing of the cerebral fluid from the lateral ventricles through the aqueduct of Sylvius, which is thus dilated, into the fourth ventricle. The symptoms of concussion are, however, essentially different from those of shock: there are both insensibility and a slow and full pulse, symptoms which are sufficiently characteristic.

The *prognosis* of shock is uncertain and doubtful. Shock may be fatal within the space of a few seconds, or the patient may live one or two days and finally die. According to Cheever, if reaction does not set in within eighteen hours after the injury, it never comes. Among the symptoms that enable us to judge best of the patient's condition may be mentioned, first, the pulse, which can be examined with the least disturbance of the patient. A patient may live in a pulseless condition for several hours, but if appropriate remedies and nursing fail speedily to restore a semblance of pulsation at the wrist, the condition of the patient may be regarded as most grave. Perhaps a more accurate guide, on account of its independence of the emotions of the patient, is the temperature. To determine the temperature properly the thermometer should be placed in the rectum. A temperature of 96° F. is regarded by Redard as indicating severe shock, and is one which contraindicates any surgical operation.

Loss of power in swallowing is considered a symptom particularly unfavorable. This indicates, according to Mansell-Moullin, an inhibition of the glosso-pharyngeal centre, which is in the immediate vicinity of other vital centres. The same import may be attributed to insensibility of the conjunctiva, indicating that the fifth pair of nerves is also implicated. Persistent vomiting, showing great irritability of the stomach, and relaxation of the sphincters, are signs that a fatal termination is close at hand.

Fortunately, in many cases much can be done toward the prophylactic *treatment* of shock. Cheever calls attention to the relation of the operative procedures of modern surgery to shock, and raises a warning voice against many of its attendant dangers. Operations under anæsthetics, often needlessly prolonged, are exhausting, and modern dressings are apt to be tedious and chilling. Great care should be taken against exposure of the patient, and a special costume is often advisable for the proper protection of the trunk or of the extremities.

Wet cloths and irrigations favor evaporation and rapid loss of heat. The axillæ, the thorax, and, above all, the abdomen, are especially prone to deleterious chilling. The prolonged exposure or the handling of certain organs, such as the brain or the intestines, is liable to produce shock. If a capital operation is to be performed upon a feeble subject, every detail of the operation should carefully be planned beforehand, and a systematic effort should be made to reduce to a minimum the time consumed in moving the patient from his bed to the operating table and back again. Many details which on ordinary occasions seem important should be sacrificed to the more important element of time. The scale may be turned at the last moment against a patient who has successfully endured the ordeal of an amputation at the hip-joint by too much attention on the part of the surgeon to some elaborate detail of suture. "The old method was a matter of minutes: now it is one of hours" (Cheever). Inasmuch as many of the features of aseptic surgery have been simplified, may we not aspire to add to modern skill the speed of a former generation?

The moment when to operate in a case of shock is a point in which the practice of different surgeons differs greatly. In cases of severe shock it is manifestly bad surgery to add the shock of an operation to that already existing, but it is often a question whether the presence of a mangled and bleeding limb does not retard or prevent reaction. While waiting for operation the patient lies upon the table, the limb is encircled by the tourniquet, and the repose and care so important to him at such a crisis cannot be obtained. More harm, however, is done by early operations than by prolonged waiting. A few hours of such rest and treatment as can be obtained often enables the patient to regain sufficient power to carry him safely through the ordeal of an operation.

Whatever is done at this time should be so planned as to avoid scrupulously all unnecessary fatigue. Rough handling and frequent shifting of the patient are manifestly out of place "when a feather turns the scale." Paget says: "There is perhaps no case in the management of which the courage to do little is more needed. Great energy of treatment may do great mischief."

The patient should be placed as quietly and as gently as possible on the bed where he is to remain permanently until reaction is established. The foot of the bed should be raised, so that the weak heart may be able to nourish the exhausted vital centres with blood. Next in importance to perfect rest is the application of heat to the body. Hospital operating tables should be so arranged that diffused heat may be brought in contact with the patient during the operation and the previous period of waiting. Heat should be applied to the extremities and to the neighborhood of the heart. Great care should be taken, particularly in the case of the patient under anæsthesia, to avoid burning the skin. An arrangement by which dry heat could be conveyed from the hot-air register to the bed itself would accomplish this object better than in any other way, and would have the great advantage of avoiding disturbance of the patient.

In cases of severe shock it is thought advisable by some to perform "auto-transfusion;" that is, to bandage the extremities so that the circulation may be limited to a confined area where the organs most essential to life are situated. Such a method involves dangerous handling, and its employment should be advised in exceptional cases only, when other and better remedies are not available.

Transfusion is now abandoned, but there may be resorted to, in cases of shock attended with great loss of blood, infusion of a warm salt solution:

Sodii chlorid.,	ʒiss.
Sodii bicarb.,	gr. xv.
Aq. dest.,	Oij.—M.

The salt solution may be introduced either into the median cephalic vein or into the loose subcutaneous tissue of the abdominal walls. Patients endeavor to supply the deficiency of fluid at the vital centres by drinking large amounts of water. If the water is well borne, there is no objection to its use, but in an irritable condition of the stomach it is not likely to be retained.

Enemata of water are very valuable under these circumstances. Mumford recommends hot enemata of a weak salt solution. A quart might be given, and be repeated in half an hour. The solution in the exsanguined state of the patient is absorbed with astonishing rapidity from the lower bowel. Lange administers a pint of water of the temperature of the body, with the addition of some stimulant, mostly claret, during long operations. This allows of absorption before it is too late. Later, there may be given nutrient enemata largely diluted—peptonized beef-juice, milk, and eggs—up to four or five ounces, with the addition of half a pint or more of warm water. The enema should be administered through a flexible catheter attached to a short rubber tube and funnel. By this means high injections may be given.

Stimulants given by the stomach should form an important element in the treatment of shock. To strengthen the heart's action, and at the same time to relieve nausea, black coffee should be given in small and frequent doses; it may be given alone or in conjunction with brandy. In giving alcohol care should be taken not to overload the stomach. Champagne or brandy and soda is often well borne. Brandy may be injected hypodermically when the emergency is great, but it should not be regarded as a matter of routine, and should only be used when other and more efficient means of stimulation, such as have already been mentioned, cannot safely be employed. The writer is somewhat sceptical as to the absorption of remedies injected into the subcutaneous tissue of an extremity during severe shock. The thick fatty layers which underlie the integument of the thorax and abdomen are more suited for hypodermic medication.

Of drugs, opium is probably the most valuable. In small doses it is stimulating, and it brings about a condition of repose which is of the utmost value. It should be given subcutaneously or by the rectum. Digitalis is also a powerful cardiac restorative: as it is not usually well borne by the stomach, it may also be administered subcutaneously or by enema. It should be given in large doses if used at all. Nitro-glycerin also strengthens a failing heart. It may be given in doses of $\frac{1}{200}$ gr., and is often of service when digitalis fails to produce the desired result. Strychnine may be placed upon the list of drugs available in such emergencies: it is highly prized by Grœningen. A good diffusible stimulant is aromatic spirits of ammonia, which has the advantage of being well borne by the stomach. It is a useful drug to employ in the least grave forms of shock.

Remember always that the condition the surgeon has to deal with is one of exhaustion, and that rest is needed for repair.

XII. FEVER.

To have a clear understanding of the nature of the process known as *fever*, it will be necessary, first, to study the laws governing the mechanism which maintains the human body at a constant temperature. The normal temperature of a human being in a state of health is 37° C., or 98.4° F., and it possesses this peculiarity, that under most varied conditions, in the tropics and in arctic regions, there is an extremely slight variation from these figures. The stability of temperature observed in man is shared by birds and mammals, and the arrangement by which this standard is preserved is known as *thermotaxis or heat-regulation.*

The body constantly produces heat by a process of combustion, oxygen being introduced into the tissues and carbonic acid being eliminated. Enough heat is thus manufactured to raise the temperature of the body 1° C. in half an hour. Were there not at the same time a corresponding loss of heat, the temperature would rise 48° C. in twenty-four hours—a height which would be incompatible with life.

To maintain a proper temperature it is necessary, therefore, that there should not only be a given production of heat and provision made for a continuous dissipation of the same, but there must also exist a mechanism by which the two processes are balanced, so that the temperature shall remain at its normal height.

If the production of heat should at any time exceed the loss, the temperature would immediately rise; if the production should happen to be less than the amount given off, there would be a fall of temperature. As a matter of fact, both of these processes are subject to considerable variation. After taking food there is an increase in the amount of heat produced, and a still greater increase after muscular exercise; during rest and sleep the amount produced is somewhat diminished. Under similar conditions there is a corresponding change in the amount of heat that is given off from the body. The flushed face of one who has just risen from a luxurious repast, the warmth and moisture of the skin and the increased respiration following active exercise, are indications that the regulating process is at work, and that the increased heat-production is being offset by the cooling down of the unusual amount of blood exposed on the surface to the influence of the surrounding air and by the increased evaporation.

In estimating the temperature of the body, particularly when making scientific experiments, it is important to remember that all parts are not equally warm. The body may be likened to a heated globe whose centre has a uniform temperature: a thermometer introduced gradually will grow warmer until it reaches this central point, when the temperature will become constant. The surface will have a considerably lower temperature, owing to the cooling process which is going on, and between the two there will be an intermediate layer whose breadth will vary according to the amount of cooling down the globe is subjected to. These inequalities are greatly modified by the circulating blood. If there has been an increased amount of heat produced, the warmer blood will, on coming to the surface, expend some of its heat in warming up this layer, and will further be cooled by contact with the surrounding cooler medium.

It appears, therefore, that there is an automatic arrangement which seems to protect the human body from the ordinary changes to which it is daily subjected; but that this works only within certain limits is evident from the artificial aids which are necessary to man to keep the temperature normal. Light clothing and cooling drinks favor heat-elimination when the atmosphere is unusually warm: the cool water taken internally not only lowers the temperature of the interior slightly, but also furnishes abundant fluid to facilitate evaporation from the surface. Further protection is given also to animals in the varying thickness of their furry coats or in their adipose tissue according to the necessities of the climate or the season. Some animals are less able to preserve their normal temperature than others, cats and rabbits being killed easily by cold baths. The equilibrium is less stable in children than in adults.

It will be seen that the change in the calibre of the vessels on the surface of the body is an important factor in the regulation of the temperature in man. In a heated atmosphere the vessels are dilated, the skin becomes unduly warm, and active perspiration takes place. If the air be dry, evaporation will be favored greatly, and man is thus able to bear for a short time temperatures so high that it was at one time supposed that the power to produce cold existed in the body.

If an animal is placed in a chamber heated to from 32° to 36°

C., great increase of respiration and heart-pulsation will be observed; also dilatation of the vessels of the skin, as may be seen in its ears and in other places. In a temperature of from 42.2° to 42.8° C. there is an enormous increase of respiration, the pulse cannot be counted, all the vessels are dilated, and all the muscles are relaxed; the pupils are also dilated. If kept long in this temperature, death occurs from paralysis of the heart and the vessels. Removal of the animal to a cooler atmosphere before death will be followed by sinking of the temperature below normal. This fall of temperature is due to the great dilatation of the superficial vessels, causing an excessive loss of heat. The low temperature observed after excessive burns is caused in this way, the dilatation of the cutaneous vessels being very complete, owing to the destruction of all muscular action in them. It is probably some such disturbance of the circulation that occurs previous to "catching cold," the dilated vessels on the surface allowing the blood which goes to the internal organs to become suddenly cooled. Anything that tends to weaken the contractility of the vessels, like too great care in protecting the surface of the body, would favor catching cold; whereas cold bathing exerts a protective action by restoring the tonus of the vessels. The time of the year when sudden changes of temperature occur, as in the early spring, is prolific in such affections, rather than in winter, when the cold is continuous. Although the symptoms produced by the long-continued high temperature resemble fever, yet the condition is *not* fever, for the temperature found to exist in these experiments is due to the storing up of heat in the body owing to a diminished loss, and not from an increased production. The increased chemical changes of fever are also not present.

On exposure to cold under ordinary conditions the skin becomes cooled and the heat-dissipation is considerably interfered with, as less moisture is now exhaled; and when the degree of cold is unusual the shivering bears evidence to marked muscular contraction taking place, notably in the muscles of the skin and in the blood-vessels, the skin becoming shrunken and the condition known as *goose-flesh* being produced. If the loss of heat is not sufficiently checked in this way, active muscular exercise will favor a restoration of the normal temperature by an increased production of heat. If a large amount of heat is suddenly abstracted from the body, as in a cold bath, the usual mechanism which regulates the heat-loss will not be sufficient to maintain the temperature, and it is interesting to find that under these circumstances as much as three or four times the normal amount of heat may be produced. The prompt reaction that follows the cold bath in healthy individuals is probably due to this fact. The regulation of heat-dissipation is effected by the vaso-motor apparatus: this is partly accomplished by the direct action of the changes of the temperature upon the surface of the body and partly by reflex action through the sensitive nerves. The dilatation of the vessels in a heated skin is evidently due to a vaso-motor paralysis, but the profuse perspiration which accompanies it is not so easily explained. Whether to ascribe it to hyperæmia of the sudoriparous glands or to stimulation of special nerves presiding over their functions remains still to be determined definitely.

Given a steady production of heat, regulation is effected by varying the amount of heat eliminated from the body; but if there is a long-continued or excessive loss of heat, as in the experiment of the cold bath, then regulation must be effected by increasing the amount of heat-production. Let the attention therefore now be turned to the *sources of heat-production in health.*

Many experiments show that muscular action is followed by an increase of temperature in the muscles. They constitute nearly one-half the whole mass of the body, and are said to produce four-fifths of the heat in health, and even more in fever. A comparison of the electrified and the quiescent nerve indicates the power of nerve-tissue to produce heat. Glands at the time of their function are a fruitful source of heat. It is generally conceded also that in all tissue heat is produced during the assimilation of nutritious material. Of these tissues, the muscles must be regarded as the chief source of heat, for in them the oxidation is most active. Even when at rest a large amount of carbonic acid is found in the venous blood which comes from them, and during severe muscular action the amount of carbonic acid exhaled may be increased five-fold.

There has already been mentioned an increased production of heat in the cold bath; that is, when a large amount of heat is suddenly abstracted from the body. This has been explained by an irritation of the peripheral nerves through change of temperature of the skin, producing a reflex action on the nerves going to internal organs, which nerves probably bear some relation to the oxidation-processes. The tissue-metamorphosis—or *metabolism*, as it is sometimes called—in the muscles at rest is not only affected by cold, but it can also be increased by strychnine and other irritants, and can be diminished or stopped entirely by curare. This drug paralyzes the terminal fibres of the nerves and thus deprives the muscles of their innervation; hence the bright arterial color of venous blood and the diminished gas-changes in curarized animals. In cases of paralysis the tissue-change in muscles is markedly affected.

The idea of an increase in the amount of heat-production through the nerves is not a new one. It is a well-known clinical fact that injuries to the upper part of the cord have been followed by a fall of the temperature below normal: in a case of crushing of the cord at the fifth cervical vertebra, reported by Hutchinson, the temperature fell to 93° F. In a case of injury in the medulla the temperature rose as high as 110° F. In cases of paralysis trifling disturbances, such as those of digestion, will cause an excessive rise of temperature for a short time. In cerebral hemorrhage and tumors of the brain there occasionally is a rise of temperature without other evidence of inflammation: just before and immediately after death there may be an excessive rise, the temperature exceeding 108° F.

Urethral fever has long been cited as an example of febrile disturbance produced by reflex action as the result of local irritation. When the vaso-motor nerves were studied by Claude Bernard, he thought that the sympathetic was a check-nerve to heat-production, and that the chorda tympani had the opposite function. He therefore called them "thermic nerves," supposing them to influence directly the production of heat going on in the tissues. Brown-Séquard showed, however, that the local rise of temperature in Bernard's experiments was due to the increased flow of blood to the part, and that no production of heat consequently took place.

These observations led to a series of experiments to determine whether there existed a special set of nerves which presided over the production of heat, the so-called "excito-caloric nerves." The vaso-motor centre has been placed in the lower part of the floor of the fourth ventricle by Wood and others, and it is also said by some writers to be situated in the anterior portion of the lateral columns. The best authorities are as yet divided on the question of the existence of a special set of thermic nerves, to say nothing of thermic centres, but the general drift of opinion is at present setting strongly in favor of such an apparatus presiding over the production of heat. Ott claims to have discovered four heat-centres.

Some recent observations in England have thrown light upon the mode of action of these nerves in producing heat in the muscle.

MacAlister has succeeded in separating the heat-producing or thermogenic function of the muscle from its motor function. By electric stimulation of the sciatic nerve of a frog he was able to record the rise of temperature produced simultaneously with motion. It was found after repeated stimulation that the thermometer showed no rise in temperature, while the motive power was still unimpaired. The same independence of the thermogenic from the motor function was observed in warm-blooded animals by experimenting with the influence of cold on the muscles. He concludes, therefore, that the metabolism by which motion takes place and that which results in the thermogenic function are different. The "contractile stuff" of the muscle is not the same as its "thermogenic stuff." They act differently to stimulation, to repairing influences, and to cold.

The thermogenic material which a muscle contains is consequently acted upon by nerves which keep up a process of innervation in the muscle whether at rest or in motion.

Gaskell has undertaken to show that this process of innervation is of a double character. He found, on the one hand, that the action of the motor nerves on the muscular fibres of the heart produced contractions (by means of chemical changes in the muscle) which are of a destructive nature; repeated action exhausts the "contractile stuff." On the other hand, stimulation of the vagus or inhibitory nerve is restorative: there is a repair of function of the muscle; the chemical changes are in this case constructive. The former action is called "catabolism," the latter "anabolism," or assimilating or trophic action. It is the stimulation of these nerves by change of air, agreeable surroundings, and other favorable conditions that promotes repair of the tissues and increases the appetite and weight. He infers that the thermogenic tonus of the muscle is preserved in the same way by two opposing innervations, the one tending to build up the thermogenic stuff, and the other disintegrating it by the process of oxidation. Further, Gaskell found, on stimulating the motor nerve of a quiescent muscle, that the contracted muscle assumed an electrical condition different from that of the uncontracted or negative variation, and that when the inhibitory nerve is stimulated the muscle exhibits a positive variation. It is possible that further experiment will show that on stimulating the motor nerve there will be an evolution of heat, and on stimulating the inhibitory nerve the muscle will become cooler.

From these observations MacAlister concludes that the muscles of the body have their double nerve-supply. "The one set of fibres are essentially catabolic: they set up disintegrative changes in the muscle, which are manifested first by thermogenesis, and secondly by contraction. The other set of fibres, whose path is perhaps anatomically different, are essentially anabolic: they set up reconstructive changes in the muscle which are manifested by inhibition of motion on the one hand and absorption of energy on the other."

It is thus seen *that the normal temperature of human bodies is* *maintained by the heat produced from the chemical changes which result from the innervation of the tissues*, and particularly the muscles, consisting mainly in the absorption of oxygen and the elimination of carbonic acid. The nervous mechanism presiding over this function is probably somewhat analogous in its action to that of the vaso-motor system, by means of which the elimination of heat from the body is effected. The stability of air-temperature is largely maintained by variations in the amount of heat-dissipation, consequently by changes in the circulation in the surface of the body and by evaporation from the skin and the lungs. Changes in heat-production are occasionally also brought about by reflex action. Whether this action is accomplished through a special regulating centre is doubtful: it is more probable that the nervous action thus aroused is exerted through thermic nerves than through the vaso-motor system, as many good observers still suppose.

The reader is now prepared to consider the *nature* of that form of constitutional disturbance which is accompanied by the *group of symptoms associated with the name of fever*. The most prominent and constant of these symptoms is the *rise of temperature*. Although it has long been recognized that the body was warmer in fever, and although as early as the last century it was discovered, by means of a Fahrenheit thermometer, that the temperature was raised even during a chill, it is only within the recollection of the present generation of physicians that systematic measurements of the temperature were undertaken, and that the relation of pyrexia to fever became generally recognized.

Perhaps the earliest symptom of fever is that general sense of lassitude and discomfort known as *malaise;* but if the patient be examined by the physician at this time, it will be found that there is already a slight rise of temperature and an increase in the rapidity of the pulse. The skin of the head and the body feels warmer to the touch, although the extremities may be cold. If the febrile attack is severe and the temperature is rising rapidly, this condition will quickly be followed by the group of symptoms known as the *chill*. These symptoms are a sense of cold, with coolness of the skin, particularly the extremities; paleness and sometimes cyanosis of the face, accompanied with involuntary movements of trembling and chattering. The duration of this period may be one or two hours, and will be followed by a sensation of undue warmth. The face will be found flushed, and the surface of the body will be considerably warmer to the touch. The patient, who at first crouches over the fire or covers himself with many blankets, now seeks relief by removing the clothing. If the rise of temperature—or the *stage of invasion*, as it is called—is gradual, the chill is usually absent. The second stage of fever, or *fastigium*, is that during which the temperature remains at its highest point. This stage may be reached in a few hours, or it may be several days before the period of invasion has been completed. The second stage is characterized by heat and dryness of the skin, by dryness of the tongue, by thirst, by scanty urine, and by headache, with more or less disturbance of the nervous system, followed by the period of *defervescence*, during which the skin becomes moist; at times there is profuse perspiration and the temperature returns to normal. During convalescence there are irregularities in the temperature, which may be slightly raised in the evening or may for a day or two keep below the normal point; the temperature being during convalescence susceptible to slight irritations. In fatal cases there may be a rapid fall of temperature, even below the normal, or in the moribund period there may be an excessive rise, which will even continue for a short time after death. The temperature varies in individuals: in children there are great changes, and it frequently runs high; in old people the rise of temperature is not so great. During the attack the patient will have lost weight, and the emaciation will be more or less marked according to the duration of the fever.

The high temperature is, as will be seen, justly regarded as the pathogenic symptom of fever, as it is more constant than any other symptom. There are, admittedly, cases in which the temperature is temporarily pushed up above the normal by a deficient elimination of heat (as in experiments to which attention has already been called), which cannot be regarded as fever, and there are also instances which have just been referred to when, owing to a great loss of heat or to fatal complications, the temperature may fall below the normal point during the progress of disease; but these conditions are exceptional. There are also some cases of excessive but temporary rise in temperature in nervous diseases, which, by some, are not regarded as febrile in nature.

How, then, shall the rise of temperature be accounted for? One of the earliest attempts to explain this rise was made by Traube, who was a pioneer in the study of the temperature in fever. His theory was based on vaso-motor disturbances, which, he supposed, caused a contraction of the arterioles on the surface of the body, thus diminishing greatly the heat-elimination. When the pyrogenic material, owing to its amount or to the sensitiveness of the vaso-motor system, makes an unusually intense impression, a rapid rise of temperature follows: in this case there would be a great difference in temperature between the central and peripheral portions of the nerves, and a chill would be the result. The fall of the temperature would be caused by a relaxation of the vessels and a consequent increase in heat-dissipation. According to this theory, no increased production of heat takes place. Since then it has, however, repeatedly been shown that there is not only an increased production of heat, but there is also an increased elimination. The warmth perceived by the hand or by more accurate thermometrical tests shows that more heat is given off than is usual. If in the mean time the temperature remains the same or increases, more heat must necessarily have been produced. The actual amount of heat produced can be determined by calorimetric test, the amount of heat-dissipation within a given time being thus determined, and the heat-production calculated after allowing for certain changes of temperature occurring during the experiment. It may, however, be determined by observing the oxidation process, as will be seen presently.

There was at first much opposition to Traube's view, but later there has been a disposition to accept the theory of a diminished loss of heat as an important factor in the production of fever. Rosenthal has recently shown that in experiments upon animals heat-loss is diminished and heat-production is not increased in fever; Maragliano found that antipyretics act by causing a dilatation of the superficial vessels, and that when the action of the drugs ceases and the fever returns this relapse is preceded by a new constriction of the vessels; Walton has shown by experiment that the symptoms of fever can be produced by a primary shutting in of heat, but he accepts, nevertheless, the view of increased heat-production in fever.

During the chill it may be assumed that there is a greatly-increased amount of heat produced, while the loss of heat is diminished, owing to the contraction of the vessels of the skin. By this contraction the heat-supply is also prevented from reaching the terminal branches of the nerves in the skin, which is the thermic apparatus by which heat or cold is perceived. According to Cohnheim, the variations of temperature are perceived by the warming or the cooling of this apparatus, and, owing to the cooling of these nerves, the sensation of chilliness is thus produced. As the heat-loss is diminished, heat must consequently be heaped up in the interior of the body, and the temperature must rise rapidly. A change of several degrees within an hour is a not uncommon occurrence under these circumstances.

Individuals whose regulating apparatus is easily disturbed are subject to slight chills from various causes. Excessive muscular action, as in mountain-climbing, may increase the heat-production three- or four-fold, and if the heat-elimination is not sufficiently active or if it is too suddenly arrested, a rise of temperature with chill may result. Such a disturbance may prove to be temporary only, but serious congestion may be caused in this way.

By the time the *second stage of fever* is reached it will be found that the temperature has ceased to rise; that the regulating process is not entirely suspended; that the spasm in the superficial vessels passes off; and that there is a free flow of blood through them. In this way the active elimination of heat is re-established. Some authorities look upon heat as an excretory product, like urea. Maclagan says: "Increased formation of any excretory product leads to a stimulation and increased activity of the organ by which it is eliminated;" consequently the increased heat-dissipation soon balances the increased heat-production, and no further rise of temperature takes place. A more careful observation of a patient at this time will show that there are great irregularities in the heat-dissipation, the surface temperature changing from hour to hour, but on the whole the amount of heat lost is much greater than that produced. It will also be found that the heat-production varies somewhat at this stage. The height of the temperature is, consequently, the result of the balance between the two.

Heat-production must not be confused with high temperature. The temperature may be high with a moderate production of heat only, owing to diminished loss of heat, and it may be low when the production is high, owing to an excessive elimination of heat.

It may be surprising to learn that the amount of heat produced in fever is really not much greater than that produced by a strong healthy man on full diet: it is, however, much greater than that produced by a well man on fever diet and at rest; but the chief point of difference in the heat-production of the sick and of the well man is, that in the latter the extra heat-production is limited to periods of active exercise or following hearty meals, whereas in the sick man the increased production is going on continually. The heat-elimination in fever is most active when the heat-production is least; that is, during the early stages and height of the fever it is irregular in its action, whereas in health the increased amount of heat produced at any time is rapidly disposed of by free perspiration; the insensible perspiration is also more abundant and constant than in fever. The two factors of heat-regulation are, therefore, acting more or less independently of one another in fever.

Coming now to the *stages of defervescence*, it is seen that the temperature is beginning to fall: this appears to be due chiefly to the fact that the production of heat is now less active. The elimination of heat is, however, greater than at any other period of the fever. Whether the perspiration seen at this time is due to the flooding of the cutaneous vessels with warm blood or to an irritation of nerves presiding over this secretion is not satisfactorily determined.

Under certain circumstances the temperature runs to an unusual height, and the condition is then known as *hyperpyrexia*, the temperature ranging from 108° F. to 110° F. This condition is explained in different ways: by some it is supposed to be caused by imperfect elimination of heat, which function has become so profoundly disturbed that the heat-production cannot stimulate it into action.

The question now naturally arises, What is the cause of the increased heat-production in fever? It was supposed at one time that local inflammation—of a wound, for instance—was the source of heat-production. The amount is, however, far too little to produce any material change of temperature. It has already been shown that the oxidation-processes are a source of heat in health, and it has long been known that the amount of carbonic acid exhaled from the lungs and of urea excreted by the kidneys is greatly increased in fever. Experiments on fever patients have shown that the amount of carbonic acid eliminated may be increased from 70 to 80 per cent., and that during the chill two and a half times the normal amount may be given off. It is only quite recently that it has been definitely determined that there is an increased absorption of oxygen going on at the same time. Elaborate observations by Lilienfeld showed that both of these gases were proportionately increased in fever—that the change was not qualitative, but quantitative. He proved also that this increase is greatest with the rise of temperature, that the interchange of these gases is somewhat less active at the height of the fever, and that during the defervescence it sinks somewhat below the normal. He further finds that the oxidation is not most active when the temperature is highest, but is most active before the latter is markedly raised and in the early stages of a rapid rise; moreover, that these processes go on just the same in fever if the temperature is kept down by some artificial means, such as a cold bath. He therefore concludes that the increased combustion in fever is not the result of increased temperature—that it can, indeed, take place independently of the latter—but that it is one of the factors which combine to cause the rise of temperature. There is also an increased amount of urea usually excreted before the rise of temperature begins, which is additional proof that metabolism precedes fever.

Lilienfeld further found that in the cases in which the temperature was kept down by the cold bath the oxidation-processes were more active. This corresponds with what has been observed in health when a man is placed in a cold bath, and is further proof that the regulation of the body-temperature continues in fever as in health, although not so accurately.

It has already been shown that the heat-production of fever is not much greater than that of a man in health with active work, and the same is true of the amount of carbonic acid eliminated from the system.

The increase in the amount of urea excreted, and other facts, point to the breaking down of albuminous products in fever. Precisely how much these nitrogenous compounds contribute to the production of heat is not determined, but it is generally conceded that the increased production of heat is due to the active combustion taking place, and particularly to the oxidation-processes that have been described. The question which now remains to be settled is the seat of the oxidation-changes and the way in which they take place.

It was originally supposed that the blood was the seat of these changes, and that fever consisted in an inflammation of the blood—a hæmitis. The increased oxidation in the blood is, however, more apparent than in the normal state: some think the blood and abdominal viscera have, in fact, no appreciable participation in the metabolism in fever. In many cases of fever evident changes take place in the blood, due to the action of pyrogenous material and micro-organisms. The breaking up of red corpuscles causes an increase of coloring matter in the urine; the chemical examination of the blood in fever has not yet produced any important results. In some fevers are found the buffy coat and a delay in the coagulation; under some circumstances a great diminution of the fibrin, particularly in animals after the injection of putrefactive substances; also a diminution of the red corpuscles and an increase of the white corpuscles, or, again, the white corpuscles may be greatly diminished, in which case there is a great increase of the fibrin element, which so raises the coagulability that dangerous capillary thrombosis may take place. It is probable that the elements which disappear from the blood are destroyed there by combustion, which is the result of the fermentative changes going on in the blood, and consequently that the blood also is a source of heat. The amount of heat, however, produced by the blood and the glandular tissue is probably small.

It has already been seen that in health the muscles are the chief sources of heat. Thermo-electric experiments show that in fever in animals the temperature of the non-contracted muscles as well as of the iliac vein is higher than the arterial blood coming from the left heart, while in the normal animal it is lower. It is evident, therefore, that heat-production in fever is increased in the muscular tissue even when at rest.

These and other experiments justify the assumption that the innervation of the muscles is the cause of the increase of the oxidation-process in animals in fever, and, moreover, that it is through the nerves that the pyrogenous material produces the increased combustion in fever. H. C. Wood confirms this view, that fever is the result of a disturbance of the nervous system. As the result of his experiments he concludes that "there are nerve-centres which are directly concerned in the thermogenic function, and which affect the production of animal heat independently of the circulation by direct action upon the tissues."

A word of explanation in regard to these nerve-centres, about which so much difference of opinion has existed, may be appropriate here.

Two kinds of nerves have been described—the excito-caloric nerves, which being irritated produce heat; and the inhibitory or moderating nerves, which restrain the action of the caloric nerves. As yet no definite information has been obtained as to the precise centre for heat-regulation, but it is known that a vaso-motor centre exists with its double set of nerves, and that the latter play an important part in the regulation of the body-temperature.

If, now, there is an increased production of heat, there must be supposed an increased action of the excito-caloric or the "catabolic" nerves, with increased oxidation and a diminished action of the inhibitory or the "moderating" or the "anabolic" nerves, with diminution of the constructive or building-up processes. If this increased action of the heat-producing nerves continues, the vaso-motor mechanism is next called into action, and for a time it may be able to regulate the temperature. This apparatus eventually becomes unequal to the task, and a rise of temperature is the result, or from the outset its action may be so altered, owing to the disturbance of the heat-regulating centre, that the vessels contract and the rise of temperature takes place more rapidly. If the heat-eliminating function is profoundly disturbed at any time—that is, if the inhibitory nerves are paralyzed and the vaso-motor nerves are unable to dispose of the accumulated heat—there will be an unusually high temperature, or hyperpyrexia. This is the *neurotic theory of fever*. It must not be forgotten, however, that many still think that the *combustion theory*—that is, that increased heat-production may take place by increased oxidation of the tissues independently of the nerves—is sufficient to account for most cases of fever; but this view hardly seems in accord with the latest and most reliable investigation.

Having discussed the *nature* of fever, it will be proper to give a few moments' consideration to its *cause*. It will not seem surprising, therefore, from what has been said, that fevers of purely nervous origin may occur, as, for instance, febrile attacks following fright or in the course of purely nervous disease. Urethral fever has already been cited as an example of fever occasionally produced by reflex irritation of the nervous system.

In the large majority of cases, fever, particularly the surgical form, is due to the presence of some foreign substance in the blood. The pioneers in investigating these substances were Billroth and Weber, whose injections of pus and putrefactive materials into the blood of animals were followed by marked febrile disturbance. They also injected purely chemical substances which were supposed to be agents in the putrefactive process, such as butyric acid, leucin, and ammonia salts, with similar results. It was found, further, that very small doses produced the same result, whereas large doses of such substances as sulphide of ammonium, carbonate of ammonia, and butyric acid depressed the temperature. The severity of the fever appeared to depend upon the quality of the virus rather than its quantity. Fresh pus and pus-serum and dried pus have all been found to be pyrogenous, but pus stagnating for a long time in the body, like that found in cold abscesses, does not possess this quality. It was finally discovered that the active properties of this class of pyrogenous substances were due to the presence of bacteria. Exactly how bacteria cause the febrile irritation, whether by the chemical changes they bring about in the blood during their development, or whether by their simple presence there, has not fully been determined. It is known that many surgical fevers are due to the presence of a chemical substance, a ptomaïne, in the blood and tissues absorbed from wounds when putrefactive changes are taking place due to the presence of bacteria.

Genuine fever may, however, take place without the action of bacteria. Febrile disturbance may occur in cases where perfect asepsis has been preserved and the wound is healing by first intention. Subcutaneous injuries, such as simple fractures, contusions of joints or of the soft tissues, are often followed by fever. Transfusion of blood, of hydrocele fluid, and even of pure water, was found to be followed by fever. In the breaking down of the protoplasm of cells there are liberated ferment substances that are similar to those described as fibrin-ferment, a substance found in the blood. In blood removed from the body this ferment substance is liberated, and the injection of this blood into the circulation of an animal may cause extensive and even rapidly fatal thrombosis. Weak solutions of this ferment substance when injected will cause a rise of temperature. Other ferments, such as pepsin and pancreatin, have been injected into the blood and have caused fever. The milder forms of fever, such as occur in aseptic wounds, simple fractures, and subcutaneous injuries, are produced by ferment-like substances which differ slightly from those produced physiologically. Substances which, chemically, differ greatly from the chemical combinations found in the fluids and tissues of the body, as the ptomaïnes, produce when absorbed severe forms of fever. Bacteria are found in the blood and the tissues of the body in the severer forms of traumatic infective disease. *In general it may be said, therefore, that fever is due to the presence in the blood of a pyrogenous substance of an organic nature that may have been produced by bacteria; or to the presence of bacteria; or, finally, to some ferment-like substance which has resulted from cell-disintegration.*

The question has been raised whether the increased temperature in fever is the result of an effort on the part of the body to protect itself against invading organisms—whether, in other words, it is the result of a struggle for existence between the body and the bacteria. It has been argued that such a widespread condition common to man and all warm-blooded animals would not otherwise exist. It would need much more light than we now have to determine whether this is the case, or whether the organism has so far gained the victory that it has been able to bring about such reactions as are favorable for its well-being. (See Hankin, p. 153.)

XIII. SURGICAL FEVERS.

THE reader is now prepared to study the different types of fever that may occur during the healing process.

Traumatic Fever.—In old times, before the days of antiseptic surgery, no wound was supposed to heal without considerable constitutional disturbance. It was indeed thought essential that a brisk inflammatory reaction should follow an operation in order that the process of repair should effectually be carried out. After an amputation of the thigh, for instance, the water-dressings were removed on the second day, and a considerable discharge would be liberated and flow either through the drainage-tubes or from openings through which protruded the long ends of ligatures that were always left uncut. On the third day the sero-sanguinolent discharge would be found mingled with pus, and the amount of swelling and redness of the parts had by this time become so great that many of the stitches were cut and the water-dressings were exchanged for poultices. Free suppuration was followed by the discharge of sloughs of connective tissue, of ligatures, of fragments of decomposed blood-clots, and finally by a subsidence of the severer symptoms of inflammation, and the wound then began slowly to heal by granulation. So frequent of occurrence was this traumatic inflammation that many surgeons, particularly the French, preferred to leave the wounds entirely open, and they stuffed them with charpie, so that healing by first intention could not take place in any part of the wound, and the discharges, which were regarded as an almost inevitable result of operations, could have free vent. It is not surprising that with this local inflammation there should have been also considerable constitutional disturbance. To this condition was given the name *traumatic* or *surgical fever*, which was regarded almost as much a physiological as a pathological process, and as an essential element in repair—a healthy reaction, as it were, in its early stages at least, from the shock of the operation.

Let the symptoms of this type of fever be traced through the week following a capital operation. On the afternoon and evening of the day on which the operation has been performed no symptoms are seen that indicate the approach of febrile disturbance; on the contrary, there is an unusual pallor in the complexion, the skin is cold, the pulse is weak, and at times is easily made to disappear altogether by firm pressure of the fingers upon the wrist. The patient lies motionless in bed and groans feebly at intervals. The respirations are somewhat superficial, and there may be some nausea or vomiting continuing beyond the period of excitement which follows anæsthesia. If at this time the thermometer be placed in the mouth, in the axilla, or even in the rectum, it will be found that the record is below the normal line. This is a condition known as "shock," of which more will be said in a subsequent chapter, and a very anxious period it is to the surgeon.

By the following morning, owing perhaps to the liberal use of stimulants, to heat, and to good nursing, the pulse has become stronger, perhaps even stronger than usual, and often is less rapid than the night before; the skin is hot and dry and the cheeks are flushed. The patient has rallied well from the shock of the operation, and reaction is said to have been established. In truth, this condition should not be called reaction, it simply being a return from the condition of the night before to a purely normal state. Science has been able to show that what is now under observation is something more than the swing of the pendulum, and that, on the contrary, there is another and entirely new pathological condition to deal with. If the thermometer be placed in the axilla, there will be found a record of high temperature, 100° to 102° F., or even higher[1]. On the evening of this the second day all these symptoms will be more pronounced, and in addition there will be found a coated tongue, thirst, considerable restlessness, and a general sense of malaise, and the chances are that both on account of these symptoms and of the pain of the wound the patient will be unable to sleep. On the following morning the temperature will drop a degree, to rise only higher than before on the evening of the third day. By this time some delirium may have been noticed by the nurse. An examination of the wound on the following morning will show the establishment of suppuration, and as the wound is cleaned off by a free flow of pus the temperature will begin to drop, and by the fourth day, for the first time, a marked fall in the temperature will be found, accompanied by a disappearance of many of the uncomfortable symptoms of fever (Fig. 65). If the

[1] In taking temperature the clinical thermometer may be left three minutes in the mouth or from five to ten minutes in the axilla. In rare cases, as in severe shock, the exact temperature of the body can be determined by placing the thermometer in the rectum.

suppuration be abundant, there will be an evening rise of temperature for a few days longer. This type of fever, preceding usually

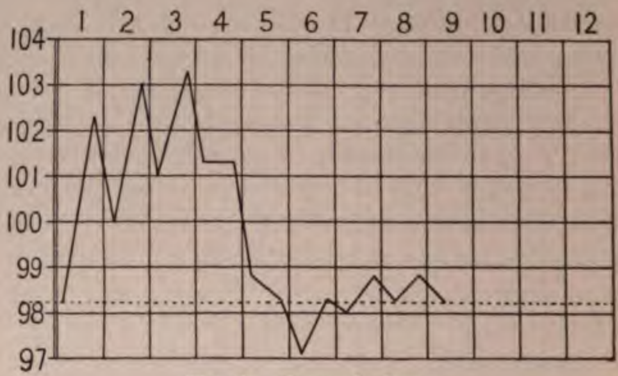

FIG. 65.—Traumatic Fever.

suppuration in the wound, lasts from one to two weeks according to the severity of the case.

The relation of the pyogenic bacteria to inflammation and suppuration has already been discussed in a previous chapter. What is of interest here is simply to determine what part bacteria play in the general disturbance of the system, or, in other words, what is the pyrogenous or fever-producing substance.

Bacteria are frequently found in the blood during surgical fever—at times the pyogenic cocci, at times other forms. It depends somewhat upon the condition of the system whether they become more numerous or are destroyed by the blood-serum and eliminated through the excretory organs. They are not present in sufficient numbers or with sufficient regularity to be regarded as the cause of fever. They are, on the one hand, rather an indication of the depressed vitality of the system, which enables them to obtain an entrance into the circulation. On the other hand, the pyrogenous action of chemical substances has fully been recognized. Further observations have not succeeded, however, in narrowing down the fever-producing qualities to any one chemical substance. On the contrary, it is probable, during the process of decomposition which is taking place in the blood, lymph, and in fragments of tissue in the wound, that quite a number of chemical substances are liberated and absorbed into the system. The substances that cause surgical fever are therefore varied in their nature.

When suppuration is established and the wound "cleans off," these ptomaïnes are washed away in the fragments which come from the wound, and the fever immediately subsides. Had the fever been due entirely to bacteria, such a change in the wound would not have produced so immediate an effect upon the system. Such organisms as are still in the circulation are eliminated quickly as soon as the system rallies from the depressing influence of ptomaïne action.

Indeed, in surgical fever the constitutional disturbance corresponds pretty accurately with the severity of the local inflammation and with the amount and quality of the secretions of the wound. A sharp rise of temperature, accompanied by delirium, by digestive disturbances, and by other signs of constitutional irritation, would almost certainly indicate the presence of decomposition in the retained fluids, the formation of an abscess, or the development of some form of infective inflammation.

Aseptic Fever.—When the antiseptic treatment was introduced it was expected that wounds healing by first intention, and consequently devoid of septic contamination, would unite without any febrile disturbance. In aseptic wounds the signs of inflammation are almost completely absent: there is but slight swelling; the surface of the wound is natural in color; the serum flows away almost in the condition in which it escaped from the vessels, slightly turbid, mixed with white corpuscles or tinged with red, and devoid of odor. It is mild and unirritating in character.

It would be natural to suppose that under these circumstances there would be a corresponding absence of all reaction upon the system. It was found, however, that a considerable rise of temperature took place after aseptic operations, without any local changes sufficient to account for this rise. It is true that occasionally, in properly-conducted operations, great tension of the stitches, imperfect drainage, sloughing of the flaps, or some irritation arising from the dressings was found, but more frequently no imperfections of this kind were discoverable.

A more careful observation of the symptoms of this form of fever showed that many of the peculiarities of surgical fever were wanting, and, in fact, that there arose a new type of fever—the aseptic fever.

The action of the virus upon the nerve-centres—which action is so characteristic of surgical fever, such as delirium, insomnia, prostration, and disturbance of digestion—is here wanting. In fact, from the appearance merely of the patient it is improbable that the presence of fever would be recognized. Such patients sleep well, can sit up in bed, and are interested in what is going on about them, or can even walk about without fatigue or other bad results. Except the rise of temperature recorded by the thermometer there is no symptom of constitutional disturbance.

It is, therefore, not surprising that many subcutaneous injuries which were supposed to produce no general impression upon the system are now found to be accompanied by a rise of temperature of several days' duration, and until it occurred to some one to take thermometric observations on this class of cases no symptom of fever, as ordinarily seen, was observed. In cases that have been operated upon there may be coating of the tongue and gastric disturbance due to the anæsthesia. The skin, however, is not so hot as in other forms of fever, and it may be moist; the urine is not diminished, and there is less loss of weight than in septic fever. The rapidity of the pulse corresponds pretty closely to the rise of temperature.

This fever, although harmless and without any special significance, may last from one to two weeks. Ordinarily, however, the temperature returns to normal at the end of three or four days.

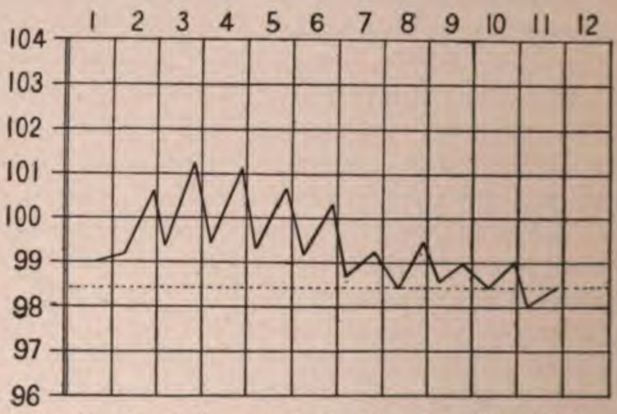

FIG. 66.—Aseptic Fever due to the Absorption of Blood-clot.

Two examples, taken from the writer's note-book of several years ago, will serve to give types of this form of fever:

1. Miss L—— was operated upon (in 1889) for a tumor of the right breast. The breast and the axillary tissues were dissected out. A deep axillary stitch and a deep breast-stitch were taken, and two bone drainage-tubes inserted, one near each suture. The dressings were removed the same evening, owing to a hemorrhage from the axillary tube caused apparently by the tearing out of the axillary stitch. A new dressing was applied, and was left untouched for several days. On its removal it was found that the wound had

healed by first intention and that the drainage-tubes had been absorbed Nevertheless, the temperature did not reach the normal line until th(eleventh day. The pulse kept pretty accurate pace with the temperature (Fig. 66).

2. In contrast with the above case may be mentioned that of Mrs. R——, whose breast and axilla underwent a much more extensive dissection. Here the stitches all held well and the walls were kept firmly in apposition, the tubes discharging the exudation which took place. The temperature rose to 99.5° F. on the evening of the second day, but with this exception it was normal from the beginning to the end of convalescence, which was rapid.

It is evident from a study of these cases that there was no absorption of septic materials or of inflammatory products, for inflammation was either absent or was present in such a mild form that it could not be regarded as belonging to the infective type. In those cases in which the temperature has been above normal there has doubtless been an absorption of certain materials which accumulated between the surfaces of the wound or at the seat of injury. These materials are blood-clot, serous exudations which failed to escape through the drainage-tubes, fragments of broken-down tissue, and minute sloughs, which, if observed under the microscope, are found to be undergoing a granular disintegration preparatory to absorption.

In a section taken from a wound in the abdominal wall the wound was found to have united, but beneath the surface of one of the lips was seen a granular mass of material which represented a dead portion of the skin about to be absorbed. Such changes are seen on a larger scale in very extensive wounds, such as amputation at the hip-joint, or in crushed wounds which have been ioroughly disinfected and are healing well. In both these cases e amount of disintegration with injury in the cellular tissue, the teguments, and even the muscles, must be considerable. Let us : what the effect of the introduction of such substances into the culation has been shown to be by experiment.

The chemistry of coagulation has already been alluded to, and reader is aware of the process by which fibrin is formed. :asionally small quantities of fibrin-ferment are liberated in the 'ulating blood by the breaking down of cells, but the vessels ear able to dispose of it and to prevent any coagulating action. :n, however, this ferment is introduced into the circulation in considerable quantity, remarkable results are found from its n. The fluid part of coagulated blood, if introduced into the 'ation of an animal, will bring about a very pronounced and sive coagulation.

From 10 to 12 cc. of blood are taken from a rabbit and allowed to coagulate into a solid cake: the fluid being pressed out and filtered, 5 to 6 cc. are then carefully injected into the jugular vein of the same animal. Immediately there occur opisthotonos, dilatation of the pupils, dyspnœa, etc., the symptoms of fatal pulmonary embolism. On examination the right heart is found full of tough clot, although still beating, and the ramifications of the pulmonary artery are distended with a red thrombus. The left heart has small-sized clots, but the blood in the remaining vessels is strikingly hard and slow to coagulate. Solutions of blood-corpuscles in ether and solution of hæmoglobin have also produced similar results. Other observers have also recorded a rise of temperature from the injection of defibrinated blood.

The same group of symptoms was also produced by watery extracts of pulverized blood freed from its ferment, which was accounted for by assuming that ferment was developed in the blood. The rise of temperature produced by the injection of water was explained in the same way. Solutions of carbolic acid were found at times to weaken, and at times to increase, the action of the ferment, particularly when strong.

Indeed, quite a variety of substances of ferment-like nature, such as pepsin and pancreatin, are pyrogenic in their action quite independently of any bacterial infection. The breaking down and absorption of the blood-clot or coagulated serum caught between the apposed surfaces of a wound or surrounding the ends of a fractured bone, or in a large hæmatoma, must therefore necessarily liberate pyrogenous substances which are readily absorbed. The same may be said of other cell-structures, as connective tissue or muscle. With the disintegration of bruised masses of tissue like these, either as the result of direct injury or from the cutting off of the circulation, there is liberated not only fibrin-ferment, but doubtless also other substances slightly altered from their original composition during life, which substances, when absorbed, produce a rise of temperature. Their close relationship to living substances renders them less intolerant to the system than the more virulent substances manufactured by bacterial action; consequently we fail to observe many of the more disagreeable symptoms of fever. These homologous substances appear to have the power to act upon the thermic centres, but to cause little other disturbance in the economy.

When a large wound heals with a minimum amount of fever, as in the amputation of the breast above alluded to, the adjustment of the wound has been so perfect that no blood-clot forms between its lips: the incisions have been cleanly cut with the knife, and no fragments remain behind to be absorbed. The effusion of serum that always occurs in greater or lesser quantity is either checked by the firm pressure of the dressings or is conducted off immediately through the drainage-tubes. Many compound fractures which have been thoroughly cleaned of clot and properly drained heal without rise of temperature, while a simple fracture may show a fever-curve of several days' duration.

There are, however, many slight disturbances which, occurring during the healing process of a wound dressed with aseptic precautions, cause a rise of temperature, and which should not be overlooked. Great tension of the lips of the wound may cause ulceration about the stitch-holes. Minute quantities of micrococci may be found in the secretions accumulating at such spots. The micrococci are insufficient in numbers, or they are so enfeebled by the antiseptics with which they come in contact as to have the power to cause putrefactive action, but they may be able to liberate a ferment capable of producing a rise of temperature. Collections of fluid may be caused by imperfect drainage, which collections, although aseptic, are still pyrogenous.

Finally, it must not be forgotten that the powerful antiseptic agents employed are potent for evil as well as for good. The poisonous action of carbolic acid and of iodoform is now well recognized, but undoubtedly many a fatal case of poisoning by these agents has been mistaken for septic infection. The rise of temperature and the digestive disturbance, with the presence of pronounced nervous symptoms, produced by carbolic-acid absorption caused the writer to be summoned in haste to a supposed case of blood-poisoning. The dark color of the urine gave at once a clue to the diagnosis. Delirium accompanying an unusual amount of inflammation after an operation for rectocele induced the writer on one occasion to take out the stitches so early as to lose much of the benefit which might have been derived from a successful operation. The cause of the trouble was subsequently found to be due to the excessive use of iodoform powder by an over-zealous nurse.

Surgical Scarlet Fever.—Many drugs are apt to cause eruptions which, in some cases, resemble those of scarlet fever. This disease has, in fact, been associated closely with surgical operations, and this supposed connection has given rise to the expression "surgical scarlet fever." Observations of this kind are exceedingly numerous, and few surgeons have failed to meet with them; whereas the association of other exanthemata—as, for instance, measles—with surgical operations does not appear to occur in sufficient numbers to be worthy of special notice.

Horsley refers to the fact that scarlet fever is particularly liable to attack children recently operated upon, especially in cases where an operation has been performed for stone in the bladder or for cleft palate. Sir James Paget, who is one of the chief authorities on this subject, is confident that there is something in the consequences of surgical operations that makes patients peculiarly susceptible to the influence of the scarlatina poison. He mentions the following case:

A boy operated upon for stone had an eruption with fever exactly like that of scarlet fever the day following the operation. Two days later it began to fade, and quickly disappeared. A month later, when the wound had nearly healed, he had hæmaturia and increased mucus, with pain on micturition. Two days after this he had sore throat, accompanied with a scarlatina eruption, followed by desquamation.

Although the symptoms, in this case, of two attacks were not typical, Paget regards it as true scarlet fever. Thomas Smith had 10 cases of scarlet fever in 43 cases of lithotomy in children. This is certainly more than a coincidence. In all cases the eruption appeared on the second or third day.

The appearance of scarlet fever in puerperal women is a well-recognized occurrence, and all the symptoms are usually so well marked that little doubt is expressed about the diagnosis. The somewhat "disorderly" appearance of the symptoms in surgical cases, as Sir James Paget expresses it, has led to the belief that these cases are not genuine scarlatina, but of septic infection of the wound; and the fact that eruptions of this character are often seen in the course of pyæmia appears to be confirmatory of this view. In a monograph on this subject Albert Hoffa states that he analyzed the different forms of eruptions which occur during the healing of a wound, and recognized four types. A certain number he regards as purely vaso-motor disturbances, arising from an irritation of the sensitive nerves and occurring after operations upon parts abundantly supplied with nerves, such as the genitalia. The eruption appears a few hours after an operation for circumcision, for instance, and resembles an erythema or an urticaria, and disappears as quickly. The cases of puerperal scarlet fever are also placed in this category by Hoffa.

The next class he calls "toxic erythema." These eruptions are analogous to the medicinal eruptions (as the rash which sometimes follows the use of copaiba or antipyrine). They occur without prodromal symptoms, and usually appear from twenty-four to forty-eight hours after all kinds of operations, and even in simple fractures. The febrile disturbance is usually intense, and in children delirium or coma may accompany the eruptions. Gastric disturbance is also a prominent symptom. Toxic erythema appears as a diffused redness or as isolated large patches with comparatively clear intervals between them. It is seen only on the body and extremities, and disappears in twenty-four hours without any subsequent desquamation.

This form is the result of an absorption of the secretions of the wound—particles of tissue or fibrin-ferment—such as occurs in aseptic fever. In some of the experiments of transfusion in animals patches of eruption are noticed. It is a not uncommon occurrence to find transitory erythema during etherization. The eruptions of carbolic-acid and sublimate poisonings would belong in this category. Hoffa reports the case of a boy whose resected knee-joint wound was syringed out with a 1: 1000 solution of sublimate. Half an hour later the patient had a chill accompanied with fever and typical scarlet rash on the whole body that lasted for twenty-four hours. The presence of mercury was afterward demonstrated in the urine and fæces.

These two varieties are strictly to be distinguished from the third form, which is infectious, and in which the eruptions are indications of a general infection of the body, occurring as they do in septicæmia and pyæmia. The eruptions are generally more marked in character and exhibit a greater variety in appearance. They may appear in the form of erythema or as urticaria. They may be diffused or be in isolated patches. The eruption may become pustular or hemorrhagic. Even purpura spots may be seen. The eruption, however, occasionally resembles the scarlet rash very closely. Sometimes—curiously enough—it affects only one-half of the body. After disappearance of the eruption desquamation may follow, and there may even be suppuration beneath the skin, with the formation of abscesses. The eruption is said to be caused by a capillary embolism of micrococci. An example of this type is reported by Ffolliott:

> A soldier in India received an extensive burn from the explosion of powder. On the third day a scarlet rash appeared. The temperature had been high from the beginning. In five days the eruption disappeared, and it was followed by desquamation. The patient had been three years in India, and in that country scarlet fever is never seen.

Konetschke reports a case belonging to this variety:

> A boy with compound comminuted fracture of the leg had septic infection of the wound. In forty-eight hours after the injury an eruption appeared,

with a rise of temperature, and remained six days, being followed by desquamation. Two weeks later a second eruption occurred, followed by desquamation, lasting only two days. One week later another eruption, with desquamation, lasting this time four days. There was some swelling of the legs each time, but no angina or swelling of the submaxillary gland, and no source of infection from scarlet fever was discernible.

Finally, in another set of cases it is evident that we have to do with genuine scarlet fever; that is, there are, in addition to the skin eruption, angina, swelling of the submaxillary glands, desquamation, and nephritis. This regularity of symptoms is not considered by Sir James Paget as necessary for diagnosis, for he expressly states that deviations from the typical course of scarlet fever are common, one or more symptoms being absent.

Another point upon which a difference of opinion appears to exist is the origin of the attack. Hoffa is inclined to think that the disease enters the organism through the wound, and cites cases to show that the eruption often begins at the edges of the wound and gradually spreads over the body. Paget is inclined to the view that the patient may have imbibed the poison before the reception of the wound, and that the disease might not have shown itself at all unless the vitality of the system had been impaired.

A case strongly suggestive of this view occurred in the writer's own practice:

A little girl twelve years of age fell and cut her forehead against a sharp piece of furniture. The wound was cleansed and united by three sutures. That evening there was swelling of the edges of the wound and a rise of temperature. These symptoms were more marked the next morning, and on the following day a scarlet rash occurred, and the patient went through a typical case of scarlet fever. The wound healed by first intention.

It seems quite evident, as Paget says, that "a peculiar liability to contagion is induced by an operation, and that the poison produces its specific effects in much less than the usual period of incubation." It is also highly probable that direct infection through the wound occurs. Thus, Paget reports a case of a child who was seized with scarlet fever the day after an operation had been performed on her mouth. Her mother knew nothing of any source of poisonous infection, but the surgeon who performed the operation was at the time nursing his own children with the disease. Billroth reports a similar case of scarlet fever following an operation upon the tongue, and it seems probable at least that Smith's ten cases of scarlet fever following lithotomy may be examples of infection of a wounded mucous membrane by that disease. Hoffa thinks that the reason a wound seems to give a certain predisposition for the disease is because a larger dose of the micro-organisms may enter through the wound, and that patients thus become affected who are not so affected by smaller numbers of bacteria through ordinary channels. The short incubation-period of surgical scarlet fever favors this view.

One of the most striking cases of infection of the wound by scarlet fever that the writer has been able to find is the following:

A physician, apparently without predisposition to scarlatina, received a scratch with a knife at an autopsy of a case of scarlet fever. On the ninth day a rash started from the wound and followed a typical course.

A case illustrating Hoffa's theory of wound-infection is the following:

A patient with stricture and urinary infiltration and gangrene of the scrotum had, on the ninth day of entrance to the hospital, a scarlet rash starting from the wound and covering the abdomen, the breast, and the neck, to the lower third of the thighs, and remaining six days. Angina was present, also high fever. Two days after the disappearance of the rash desquamation took place. Death occurred on the eleventh day after the appearance of the rash. At the autopsy a parenchymatous nephritis was found. Four days after the appearance of the eruption on this patient, a boy in the same ward with a fractured thigh and lacerations in the perineum broke out with a rash on the limbs and face. It was followed by desquamation, but there was no angina, or albumin in the urine.

It is probably not advisable to attempt to make a differential diagnosis from all kinds of skin eruptions or erythemata that may occur in surgical practice and scarlatina. Enough, however, has been said to show that a great many cases closely resemble that disease; that a certain number, and probably the majority, of cases of so-called "surgical scarlet fever" are cases of genuine scarlatina; that some of the scarlet rashes that might easily be mistaken for the disease are cases of septic infection of the skin; that in many of these cases it is extremely difficult to decide between the two affections in making a diagnosis, and that it would be well to be on the safe side and exercise all the precautions necessary to isolate the patient.

Suppurative Fever.—The fevers thus far considered have not necessarily been directly connected with suppuration. In fact, it has been shown that surgical fever subsides with the appearance of pus. The fevers already mentioned are developed during the early stages of the healing process in wounds. They may, therefore, with propriety be called "primary fevers," although this name is not usually applied to them. The term *secondary fever* is, however, sometimes given to that form which occurs during the period of suppuration, although *suppurative fever* is the more common expression. Hectic fever (from ἑχτικός, a habit) is a name usually applied to the chronic forms of suppuration, such as accompany tuberculosis.

The high temperature usually accompanying aseptic or surgical fever rarely lasts beyond the first week. If, however, the temperature does not fall, or about the beginning of the second week there should be a sharp rise of temperature, or even a chill, then there is reason to suspect the presence of pus in the wound. If the wound be examined, undoubtedly there will be found an amount of inflammation which would account for the high temperature. The lips of the wound are red and swollen, and on removing an obstructed drainage-tube or on slightly separating the edges of the wound an escape of pus follows. If proper drainage and antiseptics are now employed, the temperature will soon fall and the febrile disturbances will disappear. If, however, parts are involved whose anatomical structure makes it difficult to effect a thorough disinfection of the wound (as, for instance, a joint), or pus begins to burrow among deep layers of muscles, as often happens in a compound fracture, the fever will continue to keep pace more or less accurately with the local condition. If the infective inflammation, which has now established itself, is of an acute type, there will be a continued form of fever with frequent marked exacerbations. Usually, however, the local inflammation yields more or less to proper remedies, and becomes less acute in character: numerous sinuses are formed running in various directions; the integuments are swollen and œdematous, but are pale and flabby, and pus discharges freely from numerous openings. Chronic suppuration is established. The fever now assumes the characteristic *remittent type of suppurative fever*. In the morning the temperature is normal or even subnormal, but in the afternoon there is a sharp rise, varying from two to six degrees. There are then the hectic flush and the other symptoms of fever. Unless the progress of the suppuration is soon checked, the constitutional disturbance produces a marked change in the appearance of the patient. Great loss of flesh and prostration result, which are aggravated by "colliquative" diarrhœa and by profuse perspiration or "night-sweats."

Emaciation becomes extreme, so that the joints have an unusually prominent appearance; bed-sores appear, and it soon becomes merely a question of the power of endurance on the part of the patient. In the most chronic forms of suppuration, such as accompany tubercular disease, this type of fever may continue for many months; the emaciation will be more gradual, but when death finally occurs from exhaustion there will be found extensive amyloid disease of the internal organs.

If in the early stages of the suppuration the surgeon gains control by free incisions and drainage and removal of the suppurating walls of the wound by the curette, by resection of a joint, or by amputation, the febrile disturbance immediately subsides. This fact shows clearly that the high temperature is due to the continued absorption of pyrogenous material from the wound into the blood, and that the material when once absorbed is no longer capable of further action, for when the supply is cut off pyrexia ceases.

The precise nature of this poisonous substance is not fully understood. It is certain, however, that bacteria are only indirectly concerned in its production. The pus-coccus is indeed sometimes found in the blood, but it is also seen in cases where no febrile disturbance exists, and its presence is quite uncertain and irregular. The amount of degeneration of tissue and destruction which such a process involves must necessarily liberate a number of pyrogenous materials which find their way into the circulation and produce fever. The extensive breaking down of white blood-corpuscles in the granulation tissue forming the wall of the abscess would alone liberate sufficient fibrin-ferment to produce considerable constitutional disturbance. The virus, therefore, must be regarded as principally a chemical one, and not essentially different from that which produces surgical fever.

The principal changes found at the post-mortem examination of such cases is the so-called "amyloid degeneration of the internal organs." It is a retrograde metamorphosis of the albuminoid constituents of the protoplasm of the cells. It usually attacks the small arteries, but extensive changes of this character are frequently seen in the spleen, the liver, the intestines, the kidneys, and the heart, and, as Billroth has shown, even in the lymphatic glands. It is supposed to be caused by the constant drain upon the body of the alkaline salts, notably the compounds of potassium, produced by the suppurative discharge.

It is important to be able to recognize the presence of such changes during life, for the existence of such a degeneration of the internal organs would clearly be a contraindication for operative interference; for the disease, when once established, is generally regarded as incurable. It would obviously be useless to attempt the radical cure of hip- or knee-joint disease by resection if such a complication existed. The condition of the liver or the spleen should carefully be looked into, and any enlargement of those organs be sought for. An examination of the urine would throw valuable light upon the presence of organic diseases of the kidney. Amyloid or albuminoid degeneration of the mucous membrane of the intestinal canal would possibly betray itself by diarrhœa, by paleness of the discharges, or by the absence of bile, and by other symptoms of disordered function.

Severe operations in the later stages of cases of long-standing suppuration are rarely attempted by surgeons of experience. It is in the early stages of suppuration that prompt interference should take place. A counter-opening in one of the lips of a wound, with insertion of a drainage-tube in acute cases, will usually suffice to prevent further trouble. When the pus begins to burrow the micrococci appear to be endowed with unusual activity, and extensive sinuses form in various directions unless further progress is checked by free openings with the knife extending to the extremity of the cavity and freely exposing its walls. The walls should then be curetted carefully to remove all bacterial growth, and should be brought into contact with antiseptic agents until healthy granulations have formed.

In compound fractures and in wounds of joints this treatment becomes at times extremely difficult to carry out, and the question of resection or of amputation is often raised. The latter operation should not, however, be proposed to the patient under these circumstances, except for the purpose of saving life. Many a poor man who has risked his life to save his leg has finally triumphed over his disease: when it is realized what a terrible misfortune the loss of a limb is to the laboring man, the surgeon may well hesitate to advise amputation unless confident that death is staring the patient in the face.

Frequently an old-standing case of suppurative cellulitis—such, for instance, as follows a compound fracture—may be much benefited by a complete change of surroundings. Removal even to another bed may be sufficient—better still, to another room or ward; and occasionally the patient may be placed for several hours at a time daily in the open air. Free stimulation and the abundant use of easily-digested food will help maintain the strength, and during convalescence the employment of iron may repair the degenerated blood-corpuscles and tissues, and may give force to the appetite and the powers of digestion.

A type of fever which may appropriately be considered here, although not strictly belonging to the surgical fevers, so called, is that which accompanies lymphangitis following a "poisoned wound." If the wound be freshly made and protective inflammation has not closed the open channels which lead from it to various parts of the body, there exist conditions most favorable for rapid absorption of poisonous substances. The route through which this absorption occurs is usually the lymphatic system, and consequently a prominent feature of the absorption is the lymphangitis which marks the progress of the poison from its point of entrance toward the centre of the body. The circumstances under which this form of poisoning is most likely to occur is the accidental wounding of the hands of the surgeon or pathologist. The cause of this type of fever is probably very similar to that which gives rise to surgical fever; that is, it is largely chemical in its nature. It is probable that a bacterial invasion also occurs to a considerable extent, but in the type under consideration bacteria do not play any prominent part, as the fever subsides quickly the moment the supply of morbid material is cut off by surgical interference. There are, however, occasions when bacteria play a more important rôle under these circumstances, but these will be considered in the next chapter.

The study of surgical fevers would not be complete without considering that variety which has so long been regarded as an example of the purely nervous origin of fever—a fever in which bacteria and ptomaïnes consequently play little or no part. The most conspicuous example which has been brought forward to illustrate the type is the so-called *urethral fever.*

It is a not uncommon occurrence for the patient, after a catheter has been passed, to have the same evening a rapid rise of temperature, ushered in by a chill. The febrile disturbance, however, soon runs its course, and a couple of days usually suffice to restore the temperature to its normal condition. Some patients are much more susceptible than others, but the occurrence of the "urethral chill" is so frequent that in many hospitals it is a custom to administer a dose of quinine immediately after the use of the catheter to ward off this complication.

Unfortunately, the fever is not always of this mild type, and may even be attended with fatal results, as the accompanying case will show:

A man of middle age was admitted to the writer's ward with a stricture of the urethra. On examination his skin was found to be covered with a syphilitic papular eruption. There was a watering-pot perineum, and on the introduction of a polished steel sound a stricture of medium calibre was encountered in the penile portion of the urethra. He was an "old stager," accustomed to urethral surgery, and bore without flinching the examination. An attempt was made to pass the sound through the stricture, which, however, would not yield, and, as the pain was severe, the attempt was abandoned. No blood was drawn. The next morning the patient's temperature was 104° F. and the amount of urine was exceedingly small. Death occurred within twenty-four hours, and at the autopsy the only lesion found was an intense congestion of both kidneys. There was no cystitis, there were no marks of violence to the urethra, and there was no evidence of "surgical kidney."

It seems difficult to interpret such a case in any other way than by assuming that an intensely powerful irritation was applied to the nerves supplying the urethra, which by reflex action produced congestion of a kidney already weakened by constitutional disease. The fever may have been due to the absorption of products liberated by the morbid changes set in action in an inflamed organ, and death was caused chiefly by uræmia.

Undoubtedly, many cases of urethral fever are due to an inflammation of the kidneys, which have become gradually disorganized by the bacterial invasion, which, starting from some urethral inflammation, has gradually, with the lapse of years, worked its way along the genito-urinary tract.

Operations upon patients with *surgical kidneys*, as such kidneys are called, are to be avoided; but even in these cases it seems probable that a powerful reflex action of the nervous system has so far affected the vitality of the organ as to enable the bacteria to exert their morbid action upon it; in other words, that the nervous system plays a not inconsiderable part in the production of the inflammatory process.

Occasionally there is seen a genuine case of acute bacterial invasion of the kidneys, which appears to be the cause of a train of symptoms such as have been sketched.

Litten not long ago reported two cases—a boy and a girl—of renal mycosis:

The boy was taken ill with a slight gastro-intestinal catarrh, and on the third day a rigor and considerable pyrexia occurred. He passed on that day about seven ounces of albuminous urine, but on the three following days passed only three ounces. The pyrexia assumed a remittent type. The liver and spleen were found to be enlarged. The patient became delirious, unconscious, and death occurred after a series of convulsions. The girl's symptoms were almost identical. At the post-mortem examinations a few bac- ... found in the liver and spleen, but the kidneys were filled with ... that they could not be injected.

The true interpretation of such cases as these may be learned in the succeeding chapters, where it will be found that the kidney is considered by some to be one of the most active organs in the elimination of micro-organisms from the circulation and the tissues of the body when once an invasion has taken place, which in the above-mentioned cases appears to have occurred from the intestinal tract.

Notwithstanding that many a supposed case of genito-urinary congestion due to nervous origin has satisfactorily been demonstrated as due to the presence of bacteria, it seems probable that not all cases can be explained in this way, and that there exist a certain number which are due to nerve-action.

The nervous origin of inflammation and fever has strongly been advocated by no less a person than Lister himself. The examples he gives are numerous and interesting. He seems, indeed, almost to take the ground that the nerves play a more important part in certain inflammations than do bacteria. Ogston vigorously opposes this theory. But it seems to the writer that Lister rightly attempted to check the growing tendency to ascribe all morbid processes to the presence of bacteria, and thus to overlook facts which give many valuable hints in the management of disease.

By way of recapitulation it may be said that aseptic fever is due to the absorption of substances so slightly altered as to resemble closely the normal tissues or fluids of the body. In other types of surgical fever, such as traumatic and suppurative fever, it will be found that, in addition to the above-mentioned causes, there is a pyrogenous or fever-producing material which is manufactured through the agency of micro-organisms and belongs to the class of substances known as *ptomaïnes.* The bacteria found in sloughing or suppurating wounds are also absorbed at the same time, but in small numbers and with no great regularity, and they do not appear to exert any special influence upon these morbid processes.

XIV. SEPTICÆMIA.

In addition to the surgical fevers considered in the preceding chapter, there are still to be studied two types of fever which, on account of their fatal character, have since early times been the subject of anxious thought and careful investigation, and have greatly stimulated modern research. Among the chief blessings that have followed the introduction of the antiseptic treatment of wounds has been the almost total abolition of these pests from hospital wards. They are, however, still occasionally seen when antisepsis has failed, owing perhaps to the nature of the wound or the very unfavorable conditions under which it has been treated. Such cases will, for instance, probably be found in hospital reports of future military campaigns, although each succeeding war has shown wonderful improvement in the success attending the efforts to eradicate preventible disease. A brief reference to these fevers will enable the reader more intelligently to study the problems presenting themselves for investigation and the results that have been obtained throwing light upon their etiology.

Billroth has well said that septicæmia bears the same relation to surgical or traumatic fever that pyæmia does to suppurative fever, each being the malignant type of the corresponding milder affection. As has been pointed out in the last chapter, surgical fever occurs in the early stages of the healing of the wound, before suppuration is established, and it is principally due to putrefactive changes of greater or lesser degree occurring before suppuration finally establishes itself and cleans the wound. In the same way septicæmia is dependent upon the contingency of septic infection of the wound with its accompanying changes, and it is from complications of this character that a fatal disease is developed in the system. When suppuration is established the materials susceptible of putrefactive change are washed away, and when a fatal form of infection occurs at this later period it will be found that the morbid process now developed, both clinically and anatomically, is very different in its nature from septicæmia: the name *pyæmia* is intended to indicate close association with the process of suppuration.

The following account briefly describes a case of septicæmia such as occurred in the writer's experience:

A young, healthy man presented himself at the hospital some years ago with a sarcoma on the dorsum of the foot. Amputation was performed at the point of election—that is, through the lower third of the tibia. The wound was dressed antiseptically, but the traumatic-fever curve was from the beginning a high one: the patient did not complain of pain or distress, but appeared to be suffering from some constitutional disturbance. The wound was opened and a thin, somewhat foul serum escaped; it was then thoroughly disinfected and moist dressings applied to favor discharge. The temperature, however, continued to rise without any remission: the patient gradually became delirious, then comatose, and died on the fourth day. At the autopsy no lesion of importance was discovered and suppuration had not established itself in the wound. Although aseptic precautions had been taken in carrying out the operation, infection of the wound took place, which infection was finally traced to a dirty sponge.

This case presents an example of an infection of the system through a wound propagating itself within the body, and progressing through a series of changes to a fatal termination, notwithstanding the efforts directed toward the removal of the poison at its point of entrance. Such a case seems to offer simple conditions for the purposes of study, but of all the surgical infectious diseases not one proved a problem so difficult to explain, and there are many points concerning the origin of septicæmia that still are obscure.

It will be necessary, therefore, to enter somewhat elaborately into a historical account of the investigations into the etiology of septicæmia, which involves a consideration of much that is of importance in the early study of the "germ-theory" of disease.

Among the earliest records of septicæmia is that of Hippocrates, who recognized it as a constitutional disturbance accompanying putrefaction in wounds, particularly head-injuries and fractures. It was known in the Middle Ages as *febris putrida*. The distinction between septicæmia and pyæmia was not carefully drawn, however, and it was not until the nineteenth century that the current name was first given to it.

Piorry first introduced the term *septicæmia* (from σηπτικός, putrid, αἷμα, blood), and, notwithstanding various changes, this name substantially has been preserved until the present time.

In the early part of the present century attempts at experimental investigation of the origin of the disease were made upon animals. Gaspard injected putrefying fluids into the tissue of animals, with the result of obtaining a disease resembling septicæmia. The blood of an animal dead of the disease thus produced was injected into another animal, and, the disease being thus transmitted, he concluded that the blood of the second animal had become infective.

In 1850, Davaine's demonstration of the anthrax bacillus in the blood of animals affected with splenic fever produced a profound impression upon the scientific world, and the sentiment of the time was strongly set in favor of the "germ-theory" of the disease.

The very able investigations, in 1856, of Panum, a Danish observer, could not be overlooked, however, and it soon became a question whether septicæmia should, after all, be reckoned among the bacterial diseases. Panum performed upon animals a series of inoculations with decomposing tissues of various kinds, such as brain, muscle, connective tissue, etc. He obtained a putrid poison which did not lose its strength by filtering, and which was not destroyed after two-thirds of it had been evaporated and the remainder subjected to a temperature of 100° C. for eleven hours. He concluded that bacteria were not the poisonous principle, but that a chemical substance existed (soluble in water) which would produce the symptoms of putrid or septic infection. The intensity of this poison he compared to the venom of serpents and to curare.

Attempts were now made to study this "putrid poison" more accurately, and Bergmann thought he had obtained from putrid yeast and decomposed blood the active principle in the form of needle-like crystals, to which he gave the name *sulphate of sepsin*, 0.01 gramme of which, dissolved in water and injected into the veins of dogs, produced gastro-enteritis.

Pasteur believed the active agent concerned in the production of septicæmia to be an organism which he called the "vibrion septique." An apparent confirmation of Pasteur's views was obtained by his filtration of blood containing the bacilli of anthrax through earthen cylinders, an inoculation of animals with the filtrate failing to produce any effect. It must be remembered, however, that anthrax is a true mycosis, the purest type of bacterial disease. Siegel, who successfully separated the bacteria from putrid fluids, showed that the injection of the filtrate into animals, although it did not produce genuine septicæmia, produced a putrid intoxication—that is, a ptomaïne-poisoning, a type of blood-poisoning.

Coze and Feltz were among the first (1865) to carry out a series of inoculations on animals. They used the blood of a person who died of septicæmia, and succeeded in inoculating into another rabbit the blood of a rabbit which died from the effects of the injection, and in transmitting the poison in this way from animal to animal.

Passing now to more recent investigations, it is found that Ogston takes the ground that infective inflammation, septicæmia, and pyæmia are all different phases of the same disease—namely, micrococcus-poisoning. In septicæmia he thinks one should not dwell too much upon the idea conveyed by the old-fashioned term "blood-poisoning," but should remember that the points where poison lodges, where the various foci of infection consequently exist, are in the tissues rather than in the blood, and that from these various sources micrococci to some extent, but chiefly ptomaïnes, pass into the circulation and are distributed over the body. If the poison is strong enough, the micrococci colonize, and there are produced the metastatic abscesses of pyæmia.

Koch injected putrefying fluids, such as blood and meat-infusions, under the skin of the back in mice. In a certain number of cases marked symptoms were observed in these animals immediately after the injection, and death took place in from four to eight hours. If blood taken from the right auricle of an injected mouse was introduced into another mouse, no effect was produced; no bacteria were found in the blood nor in the internal organs. "The animal," he says, "has died not from an infective disease, but simply from the effects of a chemical poison." This assertion was proved by diminishing the dose, the symptoms diminishing correspondingly in intensity, until they were found to be absent entirely when only one or two drops were injected.

Another group of cases, however, would begin to show symptoms after the lapse of twenty-four hours, even when less than a drop of putrid fluid had been used. Symptoms of septicæmia then developed themselves, and the animal died in from forty to sixty hours after the inoculation. Even so small a quantity of fluid as one-tenth of a drop taken from the subcutaneous œdema or from the heart of such an animal, and inoculated into another mouse, produced the same group of symptoms after the same period of incubation. These inoculations were successfully repeated through a series of seventeen individuals. Koch succeeded also in obtaining a disease resembling septicæmia in rabbits. In this case the organisms were micrococci, considerably smaller than pus-cocci. These organisms were well shown in the glomeruli of the kidney and in extravasations found on the surface of the intestines.

Here, then, are found two distinct types of disease experimentally produced: First, putrid infection or intoxication or poisoning by a chemical substance, a disease similar to that described by Duncan as *sapræmia* (σαπρός, putrid, αἷμα, blood), where the symptoms begin immediately and correspond in intensity to the dose of the poison. Secondly, septic infection, bacterial poisoning, or, as it is sometimes called, "mycosis" (from μύκης, a fungus), coming on after an interval, but progressing to a fatal termination independently of the condition of the wound. The form of bacteria is not always the same, and Koch, moreover, found that certain animals—as, for instance, the field-mouse—were quite insusceptible to the septicæmia of the house-mouse; in other words, that no one form of bacteria was found that could be regarded as the specific organism of septicæmia.

Blood-cultures taken by Rosenbach from cases of septicæmia in man proved sterile. Staphylococci were found, however, in the blood in three cases of human septicæmia. This failure to obtain a constant organism, he thinks, does not prove that with improved methods we may not be able to demonstrate its bacterial origin. As a result of his investigations Rosenbach concludes that in most cases of human septicæmia we do not have bacterial invasion; the symptoms are more likely due to the absorption of poisonous ferments or ptomaïnes.

Von Eiselberg, an assistant of Billroth, examined the blood in many cases of septic fever, and was able to demonstrate the presence of staphylococci and streptococci. Cheyne, who quotes this observation, regards it simply as an example of the accidental presence of these organisms when they were apparently doing no harm. Besser examined during life the blood of 16 patients afflicted with traumatic septicæmia, and found streptococci in 4 of them after death. They were present in the blood in 7 out of 15 cases; in the organs, in 16 out of 18 cases. This author thinks that septicæmia is produced solely by the streptococcus.

Baumgarten is in doubt as to whether the symptoms of septicæmia are exclusively due to bacterial invasion or whether some of them may not be caused by ptomaïnes. The evidence shows that the bacteria are not numerous enough to produce all the symptoms of the disease. He has not been able to get bacteria from special cultures of fragments of organs removed for that purpose. If it had been possible to find the bacteria, such a method ought to have given tangible evidence of their presence. He cannot believe that such symptoms as febrile disturbance, disorders of the nervous system, and cloudy swelling of the heart, liver, and kidneys are due to the presence of bacteria. Baumgarten is inclined to think, therefore, that the toxic element predominates and exerts a poisonous influence before the bacteria have an opportunity to multiply.

Gussenbauer recognizes the difference between septic intoxication and septic infection, but thinks that at the bedside there may generally be seen a mixture of the two types. He has repeatedly been able to make cultures of micrococci from the blood of septicæmic patients, and to observe them microscopically in the freshly-drawn blood.

According to Neelsen, in true septicæmia bacteria exist in the body, but they are hard to find. The most certain method of demonstrating them is to remove fragments of organs and to allow them to brew at bodily temperatures. He is obliged to assume in these cases that a poison of great intensity is given off by the organisms, which poison kills before they can multiply to any great extent—a sort of "toxic mycosis."

Vaughn thinks that the bacteria may produce a ptomaïne not exactly in this way, but by splitting up pre-existing and complex compounds in the body, and that, according to the latest view, each specific or pathogenic form of bacteria produces its own characteristic poison or poisons.

The opinions expressed by the authors above quoted show that surgical knowledge of the poison of septicæmia is yet incomplete. There seems to be no question about the existence of a purely chemical or ptomaïne poisoning in certain cases, for not only is the type obtained in its purity in laboratory experiments upon animals, but it is also seen at the bedside under circumstances that leave little doubt as to its true character.

A bacterial form of septicæmia is found also in animals. The difficulty in finding micro-organisms in the blood of human beings affected with septicæmia appears to be due to the fact that they are rapidly swept through the large vessels, and are therefore found in the general circulation during but brief periods of time. They accumulate, however, in the capillaries, and there have an opportunity to multiply. When the process is unusually virulent, and the conditions for the development of the organisms are therefore favorable, they may eventually be found in large numbers in the general circulation. It is for this reason that the presence of bacteria in the blood of septicæmic persons is observed only under very favorable conditions. The organism which is almost always found in the blood of septic cases is the streptococcus pyogenes, and other forms of bacteria are but rarely observed.

True septicæmia in man follows closely the progressive character of the symptoms observed in bacterial septicæmia of animals: an interval follows the moment of infection, and the disease then progresses to its fatal termination, producing its characteristic symptoms in their regular order, notwithstanding what may be done at the point of entrance of the organisms to check it. Here is a process going on inside the body independently of the wound. Whether this process is caused solely by the multiplication of bacteria, or is dependent in part upon the liberation of intensely powerful poisons, or is due to some ferment-like substance capable of reproducing itself, like the poison of the serpent, as in diphtheria and tetanus, much more extensive studies upon the human subject will be necessary to enable us to say.

Harrington reports the case of a surgeon in whom septicæmia developed after a slight injury to the finger by a needle during an operation for "purulent peritonitis, probably of appendicular origin." Death occurred on the sixth day. Pure growths of streptococci were obtained by Stone from cultures taken from the heart's blood, the liver, the kidney, the spleen, and the subcu-

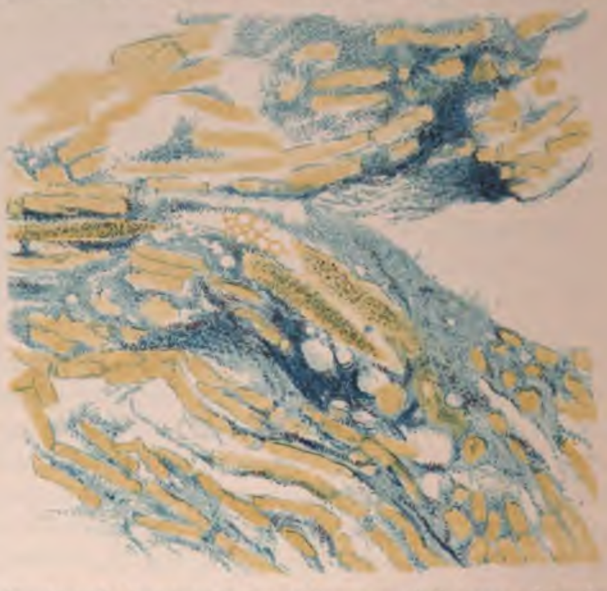

FIG. 67.—Infiltration of Muscular Tissue with Streptococci in a case of Septicæmia of Man. The blood-vessels contain numerous leucocytes, but none are found in the surrounding connective tissue.

taneous tissues of the thigh (Fig. 8). Sections of the muscles of the thigh showed that all the intermuscular spaces were distended by a mass of bacteria, and there was no infiltration of leucocytes into the tissues, though the blood-vessels seemed to contain an unusually large number of white blood-corpuscles (Fig. 67). In sections of the kidney the bacteria were demonstrated with considerable difficulty, in spite of the fact that the amount of kidney-substance that could be picked up with a small wire loop gave over one hundred colonies when planted. When found the cocci were in the intercellular spaces. Neither in the kidney nor in the muscular tissue was there any suggestion of arrangement of the cocci in chains. This was to be seen only when cultivated outside of the body.

The next point to be considered is the *mode of entrance of the poison into the body*. Of course by far the most frequent route of introduction, as the surgeon sees it, is through a wound which has become infected by the failure of antiseptic precautions in an operation or from the exposure which necessarily accompanies a severe injury.

The conditions in a wound favorable for septicæmia are those which accompany gangrene or sloughing of the tissue, although some of the most malignant types of the disease may occur when the wound has been insignificant in size. Septic infection may accompany other traumatic infective diseases, such as erysipelas and hospital gangrene, particularly the latter, and sudden putrefaction of the contents of a wound, such as is likely to occur in an infected wound containing blood-clots or imprisoned pus. Such cases as these would probably be followed by that variety of blood-poisoning known as *sapræmia*.

But it is not through wounds alone that the virus finds its way into the body. The skin is indeed a sure protection, when in its normal condition, against the invasion of microbes or ptomaïnes. The mucous membranes are not so protective in character. The intestinal canal is filled with bacteria of various kinds in its entire extent, and under conditions favorable to them they will often make a raid upon the interior of the body. In individuals of broken-down and enfeebled constitutions it is not improbable that an examination of the blood at intervals would show the presence of micrococci. As Cheyne has shown, a local injury or an inflammation will furnish a lodging for these wandering organisms, and a focus of infective inflammation will at once be established by which a general infection of the system may be produced. Chauveau has, in fact, artificially imitated such a disease by injecting putrid material into the veins of animals, and in then producing a local inflammation, such as fracture of a bone. Such cases as these are occasionally seen arising apparently spontaneously in man, and they were at one time supposed to be examples of "spontaneous septicæmia." In these cases an acute or infective inflammation is usually found somewhere to account for the constitutional symptoms. In former times these foci were often overlooked, perhaps partly on account of the violence of the constitutional symptoms, and it was therefore supposed that a sort of miasmatic infection had taken place. The origin of such forms can now be traced to various well-recognized surgical affections.

One of the commonest of these affections is acute osteomyelitis, which occurs in the long bones of the young following slight injuries or following exposure in individuals of enfeebled constitution. The onset of such inflammation is exceedingly violent, and the conditions for absorption of the virus are unusually favorable. A certain number of such cases die in the early stages of the disease before even suppuration is established. Similar inflammations may occur in other parts of the body, as will be seen presently.

It can only be assumed, by way of explanation of the origin of these cases, that an invasion of bacteria has taken place through the intestinal canal, and that they have obtained lodgment at some bruised or weakened or inflamed spot, or that the organisms have obtained an entrance through some minute wound.

But in some cases there is direct proof that an infection takes place through the intestinal mucous membrane. *Sepsis intestinalis* is now a well-recognized affection, resulting usually from the absorption of poisonous substances in food.

Vaughn gives an excellent description of the result of poisoning by eating canned meats, sausages, ice-cream, and cheese. In the latter substance he found a ptomaïne that he named *tyrotoxicon*, which is now generally regarded as the active principle in many of these cases of poisoning. This observation would place this group of affections in the class of sapræmia or poisoning by a chemical substance—an "intoxication." It seems difficult to believe that the numerous intestinal bacteria play no part in the process, and that in addition to the "intoxication" there is not also, to some extent, "mycosis" of the system. This is, indeed, the view of many observers, but Vaughn's studies led him to relegate the intestinal bacteria to quite a subordinate rôle in the process.

With regard to the respiratory tract as an avenue of entrance for the poison of septicæmia, it does not, at first view, seem probable that an example of such a mode of infection should ever occur. Ogston, however, recognizes as one of the mildest forms of sapræmia the sickness and nausea produced by a bad smell, which, as he says, is but a ptomaïne of putridity, and which under certain contingencies may produce serious symptoms. Some of the cases of fever supposed to be due to sewer gas do not differ essentially from the more strictly surgical forms of blood-poisoning. Gussenbauer suggests that the inhalation of such gases may predispose the system to the invasion of bacteria. A curious fact in this connection is the supposed immunity acquired against infection of this kind by individuals who are habitually exposed to foul odors, as those who work in the sewers or in the dissecting-room. To the surgeon such a mode of infection is comparatively rare; the physician, however, meets with it in many of the epidemic forms of disease.

Examples of infection through the genito-urinary tract occur rarely when this region is still in a normal condition. The following is perhaps such a case:

A man thirty years of age entered the hospital with symptoms of stone of a few months' standing. A phosphatic calculus of about 80 grains was removed by litholapaxy, the operation lasting twenty minutes. No blood flowed in the urine after or during the operation. Examination of the urine showed no disease of the kidneys. The patient's general health had always been good. The temperature, however, ranged in the neighborhood of 105° F. for a week, during which time the urine was loaded with bacteria. The fever gradually subsided, the bacteria disappeared, and the man made a rapid recovery at the end of that time.

Imperfect asepsis had been preserved during the operation in all probability, and infection through the urinary tract had consequently taken place. The danger of operating upon those whose kidneys are in the condition known as "surgical" is familiar to all surgeons. In this case an organ already contending with bacterial inflammation of a chronic character suddenly ceases to resist invasion as the result of the shock and depressing influence of a surgical operation or of a fresh infection.

Passing now to the *symptoms of septic infection*, the purely toxic form will first be considered, inasmuch as some authors, particularly recent writers, dwell upon the importance of distinguishing cases of sapræmia, or pure ptomaïne-poisoning, from the other forms, although the writer does not feel that we are yet fully justified in recognizing this as a separate disease in the present state of our knowledge.

The most typical example of *sapræmia* is usually found in the obstetric wards, and is there due to the putrefaction of retained clots or placental fragments in the uterus. The poison may be absorbed from the mucous membranes of the vagina or the uterus with their rich lymphatic connections, or through open wounds in the vaginal mucous membrane, or at the point of attachment of the placenta, or through the uterine sinuses directly into the circulation. The preliminary chill, which usually marks the onset of many acute forms, is generally wanting. There is, however, a rapid rise of temperature to 101° or 103° F., rarely higher. The changes in the blood are marked, the patient becoming anæmic; there is some leucocytosis, but the chief change is in the number of red corpuscles, that varies directly with the degree of blood-poisoning. In the early stages there is headache with nausea and vomiting, and later diarrhœa and purging.

The blood, the nervous system, and the intestinal canal appear to be the parts chiefly attacked by the poison. The inflammatory condition of the intestinal canal may be due in part to an effort of the system to eliminate the virus. The temperature is continuously high, and delirium supervenes, followed by coma in fatal cases.

In no disease are the results of treatment more striking and satisfactory than in this, a prompt removal of the putrefying contents of the uterus being followed in a few hours by a fall of temperature, a disappearance of all alarming symptoms, and a return to a comfortable condition.

The removal of the clots or placental remains can be effected either manually and instrumentally or by an antiseptic douche, which should carefully be introduced into the interior of the uterus, care being also taken against the introduction of air into the uterine sinuses. This douche should consist, according to Duncan, in cases where the state of putrefaction is advanced and the lochia consequently are exceedingly foul, in the injection of a solution (1 : 40) of carbolic acid. The writer takes occasion, however, to warn the surgeon that solutions of this strength are liable to produce symptoms of carbolic poisoning if used in large quantities or in repeated doses, and that in surgery such solutions are now used less frequently than formerly. Often a dose of ergot may alone be sufficient to evacuate the uterus, in which case it will be well to be content with a vaginal injection.

The writer has dwelt upon a subject not strictly surgical because there occurs in the puerperal state the best example of this type of poisoning, and the lesson it conveys as to treatment is so obvious as not easily to be forgotten. The surgeon cannot always expect, however, to accomplish so satisfactory a cure, for not infrequently the poison of septicæmia will be mingled with that of sapræmia, and the improvement will therefore be but temporary, unfavorable symptoms reappearing when the period of incubation has passed and when the virus is beginning to act upon the system.

Unfortunately, cases of the pure sapræmic type are rare in surgery. The condition most favorable in the wound for the development of the disease is the presence of unusually large quantities of blood-clot or serum, or of gangrenous or sloughing tissues, particularly in such situations as prevent an easy access of the pent-up materials to the surface. Such conditions occasionally occur after opening a deep-seated abscess, when large veins have been exposed, or in the peritoneal cavity after the removal of abdominal tumors.

All such fluids, if they are preserved in an aseptic condition, will produce nothing more than a slight rise of temperature (aseptic fever) if absorbed, but if allowed to remain stagnant they are, in certain situations—as in the vicinity of the intestinal canal—extremely liable to bacterial invasion, even though external asepsis has been successfully carried out. It is, therefore, highly important that thorough drainage should be provided when a tendency to oozing of blood is liable to occur, particularly in the peritoneal cavity when the wonderfully rapid absorbing action of the peritoneum has been impaired. The accompanying chart represents the fever-curve in a case of resection of the knee-joint. On the fourth day an infection of the wound occurred from a concealed sinus: opening and disinfection of the wound and sinus were promptly followed by a fall of temperature (Fig. 68).

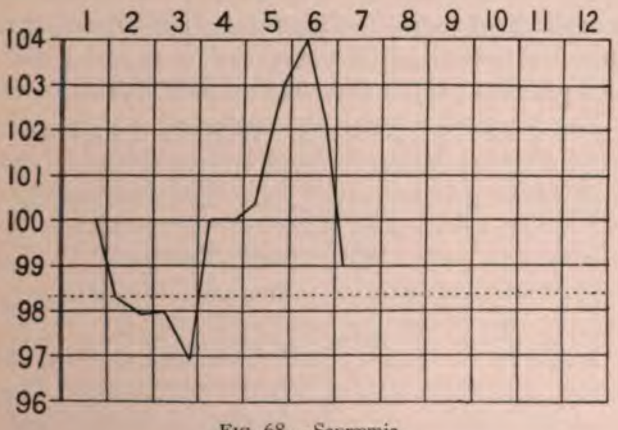

FIG. 68.—Sapræmia.

The constitutional disturbance in *true septicæmia* does not differ materially from that just mentioned in the initial stages. The main difference consists in the more gradual onset of the disease, a period of incubation existing before the presence of the virus makes itself felt. Usually after a capital operation there will be considerable elevation of temperature even in favorable cases. At the end of forty-eight hours, however, an improvement is usually expected, and for this reason, probably, there has arisen the popular belief that by the third day the surgeon is able to tell whether the patient is going to make an uncomplicated and rapid recovery or not. If at this time the temperature still remains high, or even increases, some unfavorable conditions are liable to be discovered existing in the wound, and on removing the dressing it will probably be found that a septic infection has taken place, and that one or more of the symptoms of infective inflammation are present. Occasionally the removal of stitches, or the effective disinfection and drainage of the wound, may be sufficient to arrest further constitutional disturbance, but if genuine septicæmia develops, whatever may be done to the wound will be of little avail.

With the access of fever which marks the beginning of the disease there is, as in sapræmia, rarely a chill. Great prostration with headache and loss of appetite are soon followed by a typhoid-like indifference to all surroundings, a sort of stupor which renders the patient disinclined to make complaint as to his condition or feelings. The variations in the temperature correspond more or less accurately with the local condition of inflammation in the wound, but in some of the most malignant types the wound itself may be a trivial one and the amount of local septic disturbance may be comparatively small. There is a slight morning remission, but the fever is essentially a continued one, and it increases in degree, with perhaps a rapid rise at the end of a fatal case (Fig. 69).

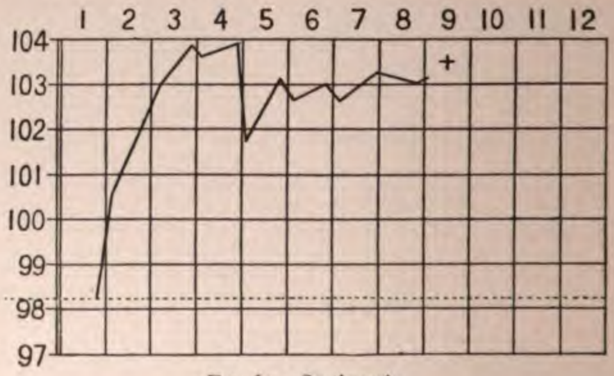

FIG. 69.—Septicæmia.

Gussenbauer calls attention to a certain class of cases in which there is subnormal temperature caused by the absorption of ammonia compounds, to which he gives the name "ammonæmia." Such a condition may be seen in connection with gangrenous hernia, and it has even been mistaken for shock. Many such cases doubtless belong to the sapræmic type of blood-poisoning, and, coming immediately after the operation or injury—such, for instance, as a penetrating gunshot wound of the abdomen—might readily give rise to such an error of diagnosis. Until Marion Sims called attention to the importance of laparotomy and to the toilet of the peritoneum in such cases, many a patient was undoubtedly allowed to die of supposed shock who otherwise might have been saved from a rapid poisoning.

The effect which the poison has upon the lymphatic system is often well marked. In some cases there is seen from the beginning an acute lymphangitis, but this symptom belongs to a class of cases that will be considered later. In those cases which do not run a very rapid course an enlargement of the lymphatic glands may be noticed, particularly in the parts communicating directly with the wound. The entire lymphatic system will be more or less affected, and this condition will show itself in an enlargement of the spleen, which occasionally may become so hypertrophied as to produce a distinct area of dulness. This is usually considered one of the characteristic symptoms of septicæmia, and should always be sought for. Another symptom characteristic of the disease is diarrhœa, which is usually not troublesome, and which can without difficulty be controlled by appropriate remedies. It is, however, frequently present, and may aid in the making of a diagnosis. At times the symptoms of gastro-enteritis are more acute, and sometimes there are rice-water discharges and vomiting, even when the route of the infection has not been through the intestinal canal, as in cases of canned-meat poisoning.

A slight discoloration of the skin, with a faint yellow tinge of the conjunctivæ, is sometimes seen in this disease, but the icterus is far less marked than in pyæmia. It is probable that the icterus is hæmatogenous, and is dependent upon the breaking down of the red corpuscles. In addition to this change in the blood there will probably also be found an increase in the number of white corpuscles and the presence of micrococci, if the blood is examined during life.

The pulse is rapid, and in dangerous cases is weak. Heart failure is a complication that the surgeon must be prepared to meet. Symptoms of ulcerative endocarditis or of pericarditis are not likely to be observed. Scarlet eruptions of the skin are not uncommon, as has been shown in the remarks on surgical scarlet fever in the preceding chapter. The character of the rash may vary greatly from simple erythema to a pustular or hemorrhagic eruption. Hoffa has obtained from the skin of patients thus affected micrococci which were not pyogenic. The eruption is explained by him as being caused by them, their presence bringing about a capillary thrombosis in the vessels of the skin. It is hardly probable that the bacteria are present in sufficient numbers to produce an actual plugging of the vessels, but they probably act upon the fibrin-ferment in a way to produce a considerable coagulation of blood in the capillary vessels. A similar condition of the vessels of the retina gives rise to retinitis, which, however, does not make itself perceptible as a symptom, but it may sometimes be detected with the ophthalmoscope.

These are the principal symptoms to be observed in severe examples of the disease. In milder forms many of them may be wanting. It is of course difficult to determine precisely when a case of surgical fever reaches that degree of severity which justifies the surgeon in giving a diagnosis of septicæmia, but undoubtedly many cases of genuine septic infection of the system are seen that eventually recover. In such cases the disease may assume a chronic form, running a course of two or three weeks' duration. A marked feature of this type is enlargement of the spleen, which may become a tumor of considerable size. The temperature does not rise so high as in the acute form.

In the more malignant cases of septicæmia as the disease progresses the wound will become unusually foul. Heuter, indeed, thought that the smell of a septicæmic patient was characteristic, and that a good surgeon ought to be able to make the diagnosis with his nose. With the powerful antiseptics of to-day he could hardly be expected to rely upon any such symptom.

The temperature continues to rise, and the skin, which is first hot and dry, later becomes bathed in perspiration. The icteric hue will now be more marked. The prostration is at this time very great, and the patient has a listless expression. Septicæmic patients are not usually troublesome; they make but few complaints even when questioned as to their feelings. Their condition has been described as one of "euphoria." There is a dull expression on the face that finally gives place to a sort of death stare, so familiar but unwelcome a sign to the unsuccessful operator. Bronchial symptoms, with quickened respiration, make their appearance, diarrhœa continues, and the stools are offensive; the urine is concentrated and scanty. Stupor is succeeded by delirium, and with the appearance of coma the patient becomes moribund.

The *post-mortem appearances* of septicæmia show but little evidence of gross change in the internal organs. A more careful study of them, however, has shown that considerable alterations exist. Putrefaction of the cadaver takes place more rapidly than in the bodies of those who have died from any other disease. The blood is of a tar-like consistency and shows little tendency to coagulate; it contains innumerable bacteria, both micrococci and bacilli. Cultures taken from the interior of the heart and from the juice of internal organs often yield a growth of streptococci. Congestion of the pia mater is often found, and sometimes also punctiform extravasations in the deeper portions of the nerve-centres. As a rule, however, there are few changes seen in the nervous system. The muscles sometimes present a brownish discoloration.

In chronic septicæmia there may be some evidence of endocarditis in a thickening of the endocardium, but the ulcerative form of inflammation is not usually seen in this disease. Slight effusions in the pericardium and in the pleura are, however, found. There may be some œdema or passive congestion of the lung, and some increase in the secretions of the bronchi. The principal change is found in the alimentary canal: here the evidences of a gastro-intestinal catarrh are marked. There is a cloudy swelling of the submucous tissue of the stomach, particularly in puerperal cases. The principal points of inflammation of the intestines, according to Gaspard, are in the duodenum and the rectum. The membrane is swollen, of a mottled color, and is dotted over with punctiform hemorrhages. According to those who have experimented upon animals, this is one of the most constant symptoms of blood-poisoning. The spleen and lymphatic glands, particularly those of the mesentery, are enlarged. The enlargment of the spleen is generally well marked, its parenchyma being much darker than usual and greatly softened. The liver shows signs of putrefaction earlier than any other of the viscera, and at times the appearance known as *emphysema of the liver* indicates an advanced stage of decomposition, with the evolution of gas. This was very marked in a case the writer once saw, in which septicæmia followed the production of an abortion produced by inserting a dirty catheter into the uterus. A slight cloudy swelling of the liver is usually all that is seen. The kidneys are somewhat œdematous, and the tubuli uriniferi are more or less affected by a catarrhal inflammation. Most observers agree that bacteria are abundantly found in the glomeruli—an evidence of the effort upon the part of nature to excrete the poison. The capillaries of an infected region are often plugged with streptococci, and the walls of larger vessels are infiltrated with them. Large numbers of these organisms are also found in the lymph-spaces of the connective tissue (Figs. 70 and 71).

FIG. 70.—Capillary Embolus of Streptococci in a Sarcoma. A round-cell infiltration is seen in the sarcomatous tissue about the embolus. (Case of fatal septicæmia.)

The condition of the wound, as might be expected, is of the foulest description. Evidences of congestion or œdema of the surrounding tissues are apparent, and all these tissues are crowded with micrococci, and they are found also in the adjacent lymphatic glands, which are considerably enlarged.

The writer has attempted to sketch the disease as it is usually seen after injuries or operations. There are, however, several variations in type which cannot be passed by without mention. Prominent among these variations is that form of septicæmia which usually follows a dissecting wound. Gussenbauer looks upon this as a form of ptomaïne-poisoning, but Horsley does not accept this view. The rapidity with which symptoms make their appearance is due not to the absorption of a chemical poison, but rather to the unprotected nature of the tissue into which a fluid in a state of active decomposition is inoculated. Then the virus selects special route, by which it is rapidly carried to a distant point. More than one case of such a poisoning has occurred to a student

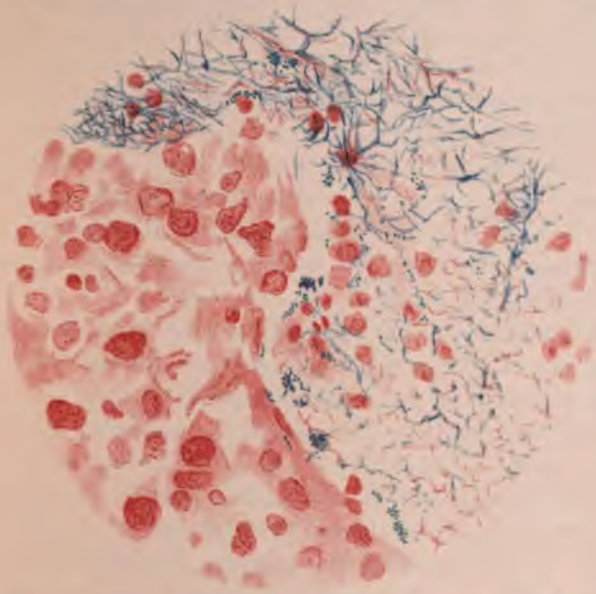

FIG. 71.—Infiltration of Vessel-wall in Sarcoma. (Case of fatal septicæmia.)

of the school during the writer's experience as a teacher. The following account gives the salient points of one of these cases:

A young man, tall and slender, about twenty-one years of age, had wounded himself slightly in the dissecting-room. He applied the next day to one of the surgeons at the hospital, complaining of pain in the shoulder. His condition was such that he was admitted to the hospital, and a consultation was held the following day upon his case. At that time the whole arm was swollen; red lines were seen running from an insignificant wound in the finger to the axilla. There was no sign of suppuration in the axillary glands, but the whole pectoral and scapular region was enormously swollen and œdematous. There was an anxious expression of countenance, high fever, and great prostration. Ether was given, and free incisions were made over the whole pectoral region, permitting the escape of a thin, slightly turbid serum. No pus was found anywhere. The patient was not benefited by the operation, and died the following day. At the autopsy no pathological changes of interest were recorded.

Happily, cases of such malignant poisoning as this are not often met with. They bear a close resemblance to malignant œdema. Usually the poison gives evidence of its presence by an inflammation of the finger extending up the hand and invading the lymphatics, as shown by red markings upon the anterior aspect of the forearm and arm. An infective, followed by a suppurative, inflammation of the glands of the axilla occurs, and with the opening of the abscess further progress of the inflammation is arrested. The fever which accompanies this attack is rapid in its onset, and may be attended with sensations of chilliness, although a chill does not usually occur. There is great mental depression, and usually there is the appearance of anæmia with great loss of strength. The constitutional disturbance yields rapidly upon arrest of the inflammation, and in the milder types cannot be called a genuine "blood-poisoning;" that is, it hardly belongs to the forms of the septicæmic or sapræmic type, but rather to the variety known as surgical or suppurative fever.

Serious forms of septicæmia accompany such diseases as hospital gangrene and traumatic gangrene. In the latter case the acute type is found in its most characteristic form, but a description of this complication is reserved for the chapter treating of Gangrene.

There has already been alluded to the so-called "spontaneous septicæmia," and it has been shown that such a disease does not exist, but that in all cases a focus of inflammation is to be found somewhere to account for the blood-poisoning. Many cases of suppuration of the appendix have doubtless passed in former times for spontaneous septicæmia. The absorption of the products of an inflammation around the appendix tainted with gangrenous and fecal extravasations must produce grave constitutional disturbance, particularly when the peritoneal cavity is invaded and this powerful absorbing surface is exposed to the poison. The conditions for acute septicæmia are here exceptionally favorable. Undoubtedly, a certain number of cases of perinephritic abscess could be rescued from this category. An individual in robust health is attacked with fever; there are no localizing symptoms; typhoid fever or pneumonia is suspected, but no characteristic signs of either of these diseases show themselves, and the patient succumbs in a few days, the strength of the poison having benumbed the senses to that extent that symptoms of local inflammation in the loin have not been complained of.

Even at the present time, when a more generally diffused knowledge and frequent autopsies have helped to clear up many obscure forms of disease, cases will occur that are still not easy to explain. The writer remembers one of this kind:

A hard-working and temperate Irishman was attacked with subacute rheumatism in the ankle. The administration of salicylic acid did not serve to check the disease, and, as symptoms of polyarticular rheumatism with increased fever began to develop, he was removed to the hospital. A temporary improvement followed, but just as the rheumatic joints were improving an intense inflammation in the neighborhood of the right hip developed, reaching from the right iliac fossa halfway down the thigh. Acute septicæmia developed, and the patient was dead before forty-eight hours had elapsed. Unfortunately, an autopsy was not permitted.

Acute osteomyelitis, which the above history suggests, has already been spoken of as a cause of septicæmia.

In making a *diagnosis of septicæmia* there must first of all be taken into consideration the condition of the wound. If there is found only an accumulation of blood-clot, the surgeon may have reason to hope that he has simply to deal with sapræmia. The high continued fever, the indifference of the patient to his surroundings, the absence of chills, and the symptoms of a general disturbance in the alimentary canal are the most important of the constitutional symptoms. The detection of an area of dulness in the region of the spleen, and of the presence of albumin and bacteria in the urine, would aid in the diagnosis. But it must be confessed that there are no constant or very characteristic local symptoms, and that our opinion must be arrived at rather by a process of exclusion.

The *treatment of septicæmia* may be either local or general. The local treatment is largely prophylactic, and consists, it need hardly be said, in a strict observance of the principles of aseptic surgery.

When once the diagnosis of septicæmia has been made, it will be the surgeon's duty carefully to examine the wound and to undertake as thorough disinfection as the strength of the patient will permit. Occlusive dressings must be abandoned; the wound must be opened sufficiently to expose all infected parts and to insure free drainage of all putrefying discharges. A thorough washing of the wound may have considerable effect upon the fever if the poisoning be largely from ptomaïnes absorbed from the secretions, and some of the older methods invented by surgeons who had a large experience in septic diseases should not be forgotten. Among these "the drip" has often done useful service—a device by means of which a constant current of fluid is carried over or through the wound. Over the part is suspended a cup from which depend a few strands of wick-yarn, and this will often prove sufficient for the purpose when a more elaborate arrangement of tubes is not possible. The antiseptic fluids applied in this way must be exceedingly weak, for a large quantity of a poisonous substance would be absorbed, even though the solution were not strong; in fact, it would be desirable to use milder remedies, like boracic acid, and to rely chiefly upon the flow of pure water. If the wound is so situated that it can be submerged in water, weak antiseptic solutions will often prove most serviceable in finally overcoming the septic infection. Carbolic solutions, in the strength of 1 : 1000 of water, or of sublimate, 1 : 50,000, will be sufficiently strong, or these solutions may be applied by means of hot fomentations or "antiseptic poultices."

Strong solutions of carbolic acid (1 : 20) or peroxide of hydrogen may be used in moderate quantities to disinfect the wound before the dressings are applied. It is probable that a very considerable amount of bacterial growth can be removed by thoroughly scraping or curetting the surface of the wound, for the most superficial growths are not only removed, but the deeper tissues also are more thoroughly exposed to the action of the disinfectants.

Iodoform, which as a dressing is at its best on such occasions as this, may be applied freely to a sloughing wound, for the danger of poisoning is less than when directly in contact with healthy granulations. It can be applied on cotton or on gauze. Whether the agent be sublimate, carbolic acid, or iodoform, a careful watch, to avoid poisoning by these agents, should be kept upon disturbance of the bowels and on the condition of the urine. The more minute details of local treatment will be found in the chapter upon Infective Inflammations.

In the general treatment of the disease the surgeon has to deal with a fever accompanied with marked prostration of the strength and a deterioration of the blood. With the introduction of the antipyretic treatment of fever this method was also employed for surgical fevers, but with most unsatisfactory results; at least, that has been the writer's experience. The relief from fever is exceedingly brief; at times no result whatever has been produced, and antipyretics do not appear to add in any way to the comfort of the patient, as is the case in typhoid fever. The disturbance of the fever-curve may also mislead the surgeon as to the patient's condition. These remedies are, however, not contraindicated in the milder forms of septicæmia, and they may often be productive of great relief to sleepless subjects. In the acute form valuable time may be wasted in watching their effect upon the disease.

Great reliance must be placed upon nourishment and alcoholic stimulants. Nourishment must, of course, be of a nature suited to the condition of the digestive system, and must be administered in small quantities and frequently. It is astonishing how much alcohol a patient in this condition is capable of absorbing without bad effects. The flushing of the face is a signal for its discontinuance or for its administration in smaller doses. The condition of the pulse will also be a good guide. Whether alcohol acts simply as a food or possesses antiseptic qualities has not been proved. According to Sternberg, the micrococcus requires the presence of 20 per cent. of alcohol for its destruction. The amount necessary to produce this action in the blood of a patient weighing one hundred and sixty pounds would be more than a quart—"a much larger quantity than the most enthusiastic advocate of its use would deem safe to administer." Alcohol to this amount has not infrequently been given in the course of twenty-four hours without ill effect, even in patients wholly unused to its action. This, of course, does not imply the presence of so large a quantity at any one time in the system; but it may be that in the living tissues the organism would find a less favorable soil for exerting its resisting powers against drug-action than when taken fresh from active artificial cultures.

Heart failure must be guarded against, and heart-tonics may often be given with advantage when the pulse is weak and rapid. The tincture of digitalis, which may be tried in increasing doses for this purpose, is a drug that should perhaps be employed more freely by surgeons than it has been.

The diarrhœa can be treated best with opium if it proves troublesome, and bismuth or tannin may be employed if necessary.

In dealing with septicæmia it must be remembered that it is an essentially different disease from the surgical fevers. The latter are due to the absorption of virus constantly generated in the wound, and it is to this point, therefore, that attention should be directed. But in septicæmia there is, except in the case of sapræmia, a constitutional disturbance which has become quite independent of its local origin—a disease in which the whole system, both blood and tissues, is involved, and which calls for the employment of all the resources at the surgeon's command.

XV. PYÆMIA.

THIS disease always accompanies suppuration, and, as will be seen, is nothing more or less than a complication of that disorder. The name *pyæmia*, which is attributed to Piorry, was not given to it until the present century (1828). It is derived from the Greek (πύον, pus, αἷμα, blood). Velpeau described the disease under the name *infection purulente*, which term is still employed by the French. Although the nomenclature is of recent origin, the disease itself was well known to the ancients, and it presents such marked clinical symptoms and pathological changes that the descriptions of the old writers leave no doubt in the mind as to the correctness of their observations.

Hippocrates described that most characteristic of symptoms, the chill, and also the existence of icterus. Paracelsus described the inflammation of the joints. Ambrose Paré recognized the fact that compound fractures of the skull were sometimes followed by abscesses of the liver. Morgagni and Petit in the eighteenth century attempted to show that metastatic abscesses were caused by an actual penetration of pus into the blood. The next observation worthy of note was that of Hunter, who recognized the existence of phlebitis as one of the links in the chain of pathological events. Hunter supposed that there took place an adhesive phlebitis which prevented the entrance of pus into the blood, although the rupture of an abscess might occasionally cause this to occur. Suppuration of the inner wall of the vein he thought was the usual result of phlebitis, by which this protective influence would be prevented, and pus would be carried away in the blood-current, or inflammation might extend along the walls of the vessels to the heart, and thus cause death. He did not, however, express himself clearly as to the relation of the metastatic abscesses to the inflammation of the veins.

Cruveilhier was among the first to point out that the result of phlebitis was the coagulation of blood in the veins. The discussion at this time turned upon the question of formation of pus by the inflamed lining membrane of the vein or by a sort of endosmotic absorption of pus through the healthy walls of the vessels.

Up to this time it was pretty generally believed that the phenomena of pyæmia were produced by the presence of pus in the blood, by whatever route it may have obtained an entrance; but as early as 1822, Gaspard made experimental observations on animals which led him to believe that the metastatic abscesses were due to the presence of putrid materials in the pus. Observations on the condition of the blood in pyæmia were numerous at this time, and the view was even advanced that inflammation of the blood itself, a hæmitis, occurred. Rokitansky described a class of cases in which, apparently, a large number of pus-corpuscles were seen in the blood, but Virchow and Bennett recognized in these cases the affection which is now known as leukæmia. A great impetus was given to the advancement of the knowledge of this disease by the investigations of Virchow upon thrombosis and embolism. That which had been supposed to be pus found in the veins near an infected wound he showed was a collection of white corpuscles; that the masses which were mixed up with them were the remains of a softened thrombus; and that embolism resulted from detachment of the fragments of such a thrombus and their arrest in some distant capillary district. If a terminal arteriole was thus occluded, infarction took place, and a metastatic abscess might be the result of the irritating nature of the materials of which the embolus was composed. This explanation fully disposed of the old idea that pus penetrated the lumen of the vein by the rupture of an abscess. At that time a great distinction was made between "laudable" pus and "infected" or foul pus, and Virchow thought to emphasize his new views on the spreading of suppuration through the body by substituting the term "ichorrhæmia" (ἰχώρ, gore, corrupted matter) for "pyæmia." What this poisonous substance was which produced such formidable complications had not yet been discovered, but light was soon thrown upon this point by the work of Pasteur on fermentation. From this time on the question of the bacterial origin of the disease gave rise to a vast amount of experimental investigation, which, however, did not succeed in clearing up this point until the methods of bacteriological study had become sufficiently perfected to give reliable results. A variety of experiments were made to determine whether the poisonous agent existed in the fluid or solid constituents of pus. Burden Sanderson, as early as 1865, injected the purulent fluid from an ankle-joint of a patient, ill with pyæmia, into the subcutaneous tissue of animals, producing metastatic abscesses. In experiments made in 1872 he found in the pus artificially-produced bacilli and micrococci, to which he gave the name *microzyme*.

Finally, a systematic study was made upon the microscopic appearance of organisms found in the pus of pyæmic patients. Doléris was one of the first to recognize in the lochia of infected puerperal patients what would probably now be called the "streptococcus," and the same organism was observed by Pasteur in fatal cases of puerperal pyæmia—the *microbe en chapelet*. He formulated the theory that the disease was due to this organism passing through the blood and lymph-channels to different parts of the body, thus producing metastatic inflammations. These organisms were reproduced by cultures taken from the blood and pus during life and after death.

Koch injected fluid from putrefying flesh into the subcutaneous tissue of a rabbit and produced metastatic deposits; from the heart of this animal blood was taken and injected into another rabbit, and the disease was thus reproduced. The organisms observed were chain-like micrococci measuring about 0.25μ in diameter. These organisms were observed adherent in small clumps to the walls of capillaries of the kidney and other organs; each little mass of bacteria enclosed several blood-corpuscles, and appeared to possess the peculiarity of causing the blood-corpuscles to adhere and form thrombi. If this is a characteristic of the streptococcus, which was probably the organism he saw, then an explanation is presented of the origin of the most characteristic feature of pyæmia. Near the wound numbers of micrococci were found in the tissues and around the subcutaneous veins, and even in the walls of the veins, through which their passage could be demonstrated in many places. Owing to their peculiar adhesive properties, Koch found they did not remain long in the circulating blood, because they were soon deposited in the capillaries of the organs. No micrococci were found in the lymphatics.

Ogston's work contains a number of interesting facts bearing upon pyæmia. His idea of a single poison for all forms of surgical fever is a simple and attractive one. He says: "Between a simple localized acute inflammation on the one hand and the severest case of pyæmia on the other there exists only a difference in degree, a difference in intensity." He shows that the swelling of joints, so characteristic a symptom of pyæmia, is produced by the effusion of serum, which, when examined, does not show the presence of micrococci, but these cocci are found in the coverings of the joint or in the synovial fringes around the cartilages, and, according to Ogston, the effusion takes place from a spot where a colony exists.

Rosenbach thought that Ogston went too far in assuming that pyæmia is purely a secondary affection. He examined 6 cases of pyæmia in man by making blood- and pus-cultures during life and inoculating animals with the organisms thus obtained. In 5 of these cases he found the streptococcus both in the blood and in the metastatic abscesses of the lungs. In 2 of these cases the staphylococcus was associated with the streptococcus. In 1 case he found the staphylococcus only, and this case recovered. As the result of his investigations he divides pyæmia into two varieties. The first is that which has already been described as *suppurative* fever; that is, a fever accompanying severe and extensive suppurations and frequently terminating fatally in the acute stage. Such cases are said to have died of exhaustion. In these cases he thinks the blood-poisoning is due to the presence of the staphylococcus, much as Ogston describes, and that this kind of fever should be called "true pyæmia." It may be said here that Heuter described this form of fever as "pyæmia simplex" in contradistinction to the embolic form, which he called "pyæmia multiplex." The latter was Rosenbach's second form of pyæmia, or the "thrombo-embolic" form with metastasis, which, as he shows, may be quite independent of the condition of the wound and in active development, even after the wound has healed, and which is usually caused by the streptococcus.

A good many observations have been made upon the bacteria of pyæmia. Besser, for instance, examined the blood, pus, and parenchymatous fluids in 23 cases of pyæmia. In 8 the staphylococcus was found; in 14, the streptococcus; and in 1 both kinds of cocci were seen. During life the cocci were found in the blood in 11 out of 12 cases. Out of 46 cases, in all, collected by him, the staphylococcus was found in 22, the streptococcus in 21, and both were found in 3 cases. He concluded that there was no difference between the cocci of pus and the cocci of pyæmia. Pawlowsky examined 5 cases of pyæmia in man, and found the staphylococcus in 4. In the fifth case, which had an unusual number of joint-complications, he found the streptococcus. He believed the staphylococcus is the usual cause of pyæmia, and particularly in cases of abscess of the internal organs.

Pawlowsky, perceiving that pure cultures of the pyogenic cocci when introduced into the organism disappeared rapidly, made simultaneous injection of sterilized cinnabar particles and staphylococcus cultures into the circulation, and produced a typical pyæmia with metastatic abscess. Injections of the coccus without the cinnabar were not sufficient to produce the disease. The particles of cinnabar were supposed to have favored the formation of minute thrombi, impairing the local nutrition of the tissues and favoring impaction. Bonome also succeeded in getting metastatic abscesses by intravenous injection of fragments of sterilized pith with pure cultures of staphylococci.

An important addition to the experimental investigation of pyæmia is that intended to throw light upon the origin of the nodular and ulcerative endocarditis found in this as well as other diseases. An acute endocarditis was produced by Wyssokowitch by introducing an instrument through the jugular vein and bruising the valves, and subsequently by injecting bacteria of different kinds directly into the circulation. If the bacteria were injected into the connective tissue, or an interval of two days was allowed to pass after the lesion of the valves had been produced, or a very weak dose of bacteria was employed, the endocarditis did not take place. Ribbert succeeded in infecting the endocardium without previous injury by introducing fragments of potato with the culture. These small particles enabled the bacteria to become, mechanically, more easily arrested, and the injury inflicted upon the endothelia at the same time offered a soil more favorable to bacterial growth, owing to its impaired condition.

The process by which the endocardial lesion appears to be formed in the human subject is as follows: The micrococci become attached either to some old lesion of the valve or to some point on the valve favorably situated to receive them, owing to the pressure of the blood-column against it when the valves are closed. A coagulation-necrosis of the inner wall of the vessel takes place at the point of attachment. A rough surface is thus presented to the blood-current, and numbers of white corpuscles or blood-plaques become attached to the little clump of micrococci and necrosed tissue, and a thrombus is thus formed. If the destruction of tissue is not great, the granulation tissue may cover in the micro-organisms and a nodular mass will be found in the valve; but if there has been extensive necrosis, when the protecting thrombus is swept away an ulceration will be observed in the wall of the valve. Baumgarten suggests that the tuberous form of endocarditis is produced by the staphylococcus, and the ulcerative form by the streptococcus.

Having thus glanced over the most important experimental investigations in pyæmia, the reader is now prepared to form an opinion as to the nature of the micro-organisms and the route which they take in infecting the system.

Both the staphylococcus and the streptococcus have been observed, and, although at one time it was supposed that the former was the principal agent in producing the disease, the data afforded by observers up to the present time do not permit one to decide in favor of either: so far as can be judged, therefore, it is probable that accidental anatomical and pathological conditions determine the question of a successful resistance on the part of the tissues, rather than the presence or the absence of either of the above varieties of micrococci. Enough is known of the varying degree of virulence of pathogenic bacteria to enable one to realize that they may act very differently under varying conditions. This can easily be proved by clinical observation as well as by laboratory experiments.

The route through which an infection of the system takes place from a wound is almost invariably the blood-vessels, although occasionally the infection may follow the lymphatic system. When the micrococci are not restrained in their growth in an infected wound, they soon reach the blood-vessels, and when they come in contact with the walls of a vein an inflammation is set up and *thrombophlebitis* results. As they reach the intima a disturbance of nutrition in the endothelium takes place, and rough places are thus formed on the inner surface of the vein. If, now, the descriptions of Osler and Zahn are recalled, it will be found that a number of leucocytes become adherent to such a spot and form a little mass attached to the inner wall, which mass after a while becomes more or less homogeneous, so that the individual corpuscles cannot be discerned. The white thrombus of Zahn is formed in this way, and it becomes the starting-point of a thrombosis which may so enlarge as completely to fill the lumen of the vein. The blood-plaques, as well as the leucocytes, will also be seen collecting about this rough spot, and aid in the process of coagulation. Such an event would seem to serve as a protection to shut off the damaged vein from the general circulation. The street has been closed for repairs, as it were, and doubtless in many a case such is the result of this effort on the part of nature. Unfortunately, the thrombus affords an unusually good soil for the micrococci, and an infection and puriform softening of the clot eventually take place. Inasmuch as thrombosis may occur throughout the extent of a large vessel—as, for instance, the femoral vein (Fig. 72)—a large mass of soft material, looking like blood-clot and pus mixed together, is contained inside the vessel, extending far beyond the limits of the wound and in more or less direct communication with the circulation. The mode of progress of the micrococci from the wound to the adjacent vessels seems merely to be a process of germination and growth. It was at one time thought that they were transported into the thrombi already formed by the white corpus-

FIG. 72.—Thrombus of Femoral Vein.

cles, in the interior of which cells numbers of cocci are often found; but this theory has not been sustained. Thrombo-arteritis may also occur; that is, the micrococci may penetrate the arteries as well as the veins, but the denser walls and the more vigorous current do not favor development of thrombi; and when thrombi are found they do not, of course, spread to distant points, but fragments detached will remain in an adjacent capillary district. Fragments from the infected venous thrombi when detached are arrested in the capillary system of the lungs, where they form new foci of infection, and favor the formation of a *metastatic abscess* (Fig. 27). Very small emboli may, however, pass through the lung capillaries, as the vessels are much larger than those of other capillary systems, and in this way the whole arterial system will be exposed to a similar infection. Cocci may also be found free in the circulation independent of emboli. Their direct penetration into the circulating blood is impeded by the thrombosis which occurs at the point of entrance in the vessel-wall. Small masses of micrococci may, however, be detached before coagulation has taken place, and be swept off into the current. Single organisms are not likely to cause suppuration, as the resistance of the tissues neutralizes their pathogenic action, and they quickly disappear from the circulation.

The micrococci, when circulating through the blood, are lodged in and become attached to the endothelium of capillaries where the circulation is slow, or in the lumen of vessels with an anatomical arrangement favorable for a lodgment, as in the glomeruli of the kidney. Having reached a stationary point, they begin to grow either in the lumen or in the wall, and spread through a considerable capillary district. A necrosis takes place around the mass of micrococci, and suppuration occurs at its border. As the cocci from the centre and the pus-cells from the periphery break into the necrosed tissue, it melts down and a *miliary abscess* is thus formed. If the bacterial growth is of slight intensity and is not extensive, necrosis will probably not occur, but suppuration may take place without it. Free micrococci may also become attached to the valves of the heart and to the veins by the blood-pressure forcing them into the soft endothelium while the valve is closed, causing nodular or ulcerating endocarditis. Fragments of emboli laden with micrococci are more likely to become attached in this way, as has already been shown experimentally. If the embolus is arrested in the terminal artery of an organ, a wedge-shaped infarction will result. The tissue, thus lowered in vitality, is soon invaded by the micrococci: leucocytes also wander in, a softening takes place, and there arises a wedge-shaped abscess situated near the surface of an organ. If the lodgment takes place in a tissue with free anastomosis, the cocci invade the intermediate tracts of tissue or parenchyma, or they may spread backward along the inner wall of the artery to a collateral branch, and may thus be carried to an adjacent capillary district; in this way a more or less diffused abscess will be formed. From the above examples it will readily be seen that the great variety of suppurations occurring in pyæmia can be accounted for by the spreading of micrococci from the original wound into different parts of the body.

It will be perceived that the old idea that pyæmia was due to the presence of pus in the blood has been abandoned. It occasionally happens, however, that an abscess may be situated in the neighborhood of a large vein, and that perforation of the vessel-wall may take place, the abscess actually emptying itself into the cavity of the vessel. Schuh reports a case of a man suffering from an acute abscess behind the peritoneum. He was suddenly taken ill with symptoms of pyæmia, and died in two days. At the autopsy it was found that the abscess had broken into the ascending cava and that metastatic abscesses existed in the lungs. Numerous balls of pus were found floating in the blood, and about two ounces of pus were collected from the blood-vessels. Gussenbauer reports a number of such cases.

Infection may also take place through the lymphatic system, although the chains of lymphatic glands offer a protection which is not found in the veins. Gussenbauer reports a case of gangrene of the lower extremities in which foul pus was found in the thoracic duct; Schuh records a case of lithotomy, with death three weeks after the operation, in which case the lymphatics over the sacrum and in the lumbar region were filled with purulent material, and the thoracic duct was distended to the size of a pigeon's egg with thin green pus which was found extending up to its opening in the vena cava. Pus may be found in the lymphatics of the broad ligaments of the uterus in cases of puerperal pyæmia. In such a class of cases the richness of the lymphatic connection and the direct communications with the venous system render a general infection more probable than in the case of suppuration in more superficial regions which have access only to the peripheral lymphatics on the surface of the body.

All these forms of infection, which take their departure from a wound, have been called "types of extravascular infection," to distinguish them from a class of cases in which no wound is present; nevertheless, pyæmia exists.

The cases of intravascular infection, or the so-called "spontaneous pyæmias," have long been recognized, but their etiology has been but little understood. An otherwise healthy individual receives a trifling wound or catches cold, and after suffering from severe chills and fever, and perhaps swelling of the joints, dies, and metastatic deposits are found in the internal organs. A young man or a boy stays too long in the bath, and the next day he has a severe chill; symptoms of acute osteomyelitis of the femur develop, and he eventually dies of pyæmia. An interesting feature of these cases is that they are frequently associated with acute ulcerative endocarditis. More will be said about their clinical features in discussing the symptomatology of pyæmia.

How does infection take place in cases like these? It has been pointed out that micrococci are found in the circulation even when no suppuration takes place. All that seems necessary is a lowering of the general tone of the system or the existence of some weak or diseased spot, in order that these organisms may break down the barriers which the normal tissues afford. Under such conditions there may arise a marked disturbance of function or circulation of an organ, as the kidney, perhaps from getting chilled, or an inflammation may occur which will favor the localization of micrococci in that neighborhood, and a perinephritic abscess may be the result. A starting-point is thus established from which an extensive infection of the system may occur. The changes in the nutrition of a rapidly-growing long bone, and its anatomical peculiarities, account for the fact that such tissue is a favorite seat of infective inflammation. The rich anastomosis in the medullary cavity favors the accumulation of micrococci in a given capillary network. A rapid multiplication of the organism occurs: the vessel endothelium is first attacked, and then the intravascular tissues, and there is soon a considerable space undergoing necrosis and forming the central point of an acute suppurative inflammation. There are cases, however, in which no preliminary abscess is formed. The attack may be accompanied with no characteristic symptoms of local disease, yet an autopsy will show metastatic abscesses in the internal organs. In these cases marked evidences of ulcerative endocarditis are pretty sure to be found, and it is supposed that the micrococci have obtained a lodgment in the valves of the heart. According to Osler, the number of primary cases of ulcerative endocarditis is limited, this lesion of the heart being more frequently associated with some other affection, even with such a disease as pneumonia. Pneumococci have been found in such cases.

In pre-antiseptic days, when pyæmia was a much commoner disease in hospitals than it is now, it was thought that certain *seasons of the year* were favorable for epidemics of the disease. The writer has observed such an epidemic. Having had one or two deaths from pyæmia in his hospital wards, attention was given to the search for a local cause. To his surprise, he learned that a neighboring lying-in hospital had been closed on account of a similar "epidemic," and that several cases of puerperal pyæmia had also occurred in a suburban hospital. It was at the time of the year, the early spring, when erysipelas and other traumatic infective diseases have long been dreaded by the surgeon. In some of these affections, as erysipelas, climatic influences seem to be an etiological factor, and the writer sees no reason to doubt the existence of conditions in the atmosphere that are more favorable to the development of an unusual activity in the staphylococcus and streptococcus than at other times. So acute an observer as Sir James Simpson says: "There are epidemic states in which puerperal and surgical fevers are frightfully common. Some localities and towns are far more frequently their seat than others." The enthusiasm for antisepsis should not allow the surgeon to forget the teachings of an earlier school, founded as they were on abundant experience.

In a report made to the Pathological Society of London the statement is made that during ten years (1869 to 1878), within which period all cases of pyæmia in the London hospitals were recorded, the mortality of 1874 and 1875 was decidedly in excess of that of other years. These two years were noted for their marked meteorological conditions. In 1874 there was a remarkable deficiency of rain during the whole year. On the contrary, 1875 was characterized by its excessive rainfall. The most fatal months during this series of years were February and March.

As to the *influence of age and sex*, it may be said that children and old men, and women at all times of life, are less frequently affected than men in the prime of life. This immunity is perhaps partly due to less exposure to traumatism, but so far as children are concerned this is probably not the reason. Wounds in children usually heal rapidly, the reparative process is more active, and it effects more perfect results than in maturer years. The blood and tissues of young children are, as a rule, purer and healthier, and the resisting power against infection is consequently greater. In the adult there is present all the ailments due to advancing years, which ailments handicap him in the struggle for life; and in certain conditions of the system, such as alcoholism and diabetes, there exist conditions peculiarly susceptible to traumatic influences. Pyæmia does occasionally occur in infancy: Savory reports cases in children ten months old, and one even as young as four days old.

Among the kind of *wounds which predispose* to metastatic inflammation may be mentioned contused wounds, wounds of joints, compound fractures (supposed to favor pyæmia by fat-embolism), particularly fractures of the head, osteomyelitis, injuries of the veins or of the vascular regions, and wounds received in war or by individuals in an enfeebled condition.

The disease usually makes its appearance about ten days after the injury—that is, at the height of the suppurative process—but it may begin at any time during the suppurative process.

The most prominent of the *symptoms of pyæmia* is the chill. This chill, however, may not accompany the first onset of fever, which is usually severe. At other times the chill may be the only symptom which first arouses the surgeon's suspicion, for the febrile disturbance may be slight or may be of a degree which has existed for some time; as, for instance, in a case of suppurative fever. An examination of the wound may reveal local infection and symptoms of infective inflammation. The lips of the wound are, in this case, red and swollen, and the interior of the wound may have a discolored or grayish, sloughing appearance, but, even though the wound be far advanced in the process of repair, a typical pyæmia may develop itself: indeed, some cases have been reported where the disease first made itself manifest after the wound had actually healed. In such cases the wound is probably situated near some rich venous anastomosis, as the hemorrhoidal veins or the sinuses, in which thrombi are readily formed. *The chill* may be either a slight shivering or of the severest type, followed by profuse perspiration and considerable exhaustion. Usually after the chill is over the patient appears very much as before. There is no mental disturbance, although there may be at the same time considerable fever. Ordinarily the surgeon does not observe a second chill until the following day; although Billroth, who has made a special study of the chills of pyæmia, states that as many as three chills may occur in the course of a single day. He also noticed that chills were less likely to occur during the evening and night than in the morning or afternoon. He lays special stress upon the marked difference between septicæmia and pyæmia so far as this symptom is concerned, as in the former disease, except perhaps at the onset, chills are never seen. The explanation of the chill is to be found probably in the existence of multiple suppurations throughout the body. The surgeon is aware that when in the course of an acute inflammation, as in cellulitis, a chill occurs, there is every reason to expect the appearance of pus. In the chapter on Fevers the writer endeavored to explain the cause of a chill and its relation to sudden elevations of temperature. With the formation of each new metastatic abscess there is probably a liberation of fresh pyrogenous material, which may have a more or less specific action on the blood and tissues, or possibly the nerves controlling heat-regulation, thus producing this special form of disturbance.

A no less striking peculiarity of pyæmia are the *variations of temperature*. Billroth, who made a careful study of fever-curves in various fevers, first called attention to the curve of pyæmia. Heuter, who has also studied this question, speaks of the pyæmic curve as most characteristic.

The fever-curve which pyæmia most nearly approaches is that of intermittent fever, but it varies from the latter in lacking regularity of change. It differs from all fevers in not having a regular evening exacerbation and morning remission, although this may occur. Heuter describes it as an "irregular intermittent type" (Fig. 73). Its irregularities are certainly great. The usual course of events is as follows: There is, at the beginning, usually a sharp rise, which may reach almost the highest point of the curve. If the temperature is already high at the time of the appearance of the disease, there will be a sharp rise to mark its onset. There will be a period of pyrexia of longer or shorter duration, and then a fall, but not to the normal line, followed by a succession of similar exacerbations. During these periods of high fever the temperature remains at no fixed point, but there will be constant variation of

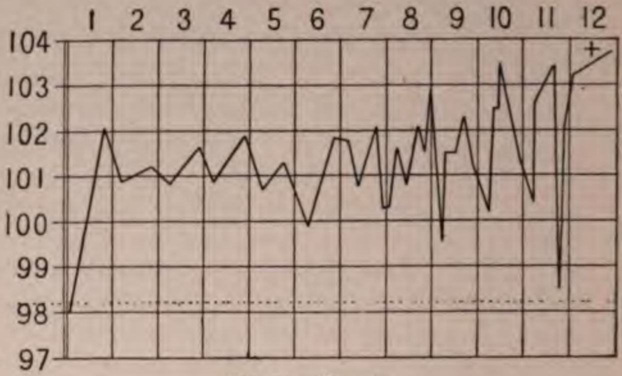

FIG. 73.—Pyæmia.

fractional portions of a degree. These variations may occur almost hourly, so that it is necessary to take thermometric observations very frequently. It is customary, when the existence of pyæmia is suspected, to take a record every two hours, which is pretty sure to bring out varying undulations in the fever-curve. At the same time the daily record of temperature carried through the period of the disease shows also the greatest irregularities. In general it might be said that the curve of pyæmia consists of an irregular series of sharp rises and falls, with an intervening zigzag outline to the curve. During all this time the normal line is not reached, yet in exceptional cases the temperature may return to normal, and may remain there for a day or two. Occasionally there has been observed a sharp rise post-mortem. The reasons for these remarkable changes are naturally to be sought for in the diverse pathological appearances which are found at the autopsy. There may not always be an abscess to account for each chill or a chill to correspond to each abscess. Individual susceptibilities doubtless play an important rôle in the development of this symptom, but the multiple foci of embolism, infective inflammation, and suppuration, some visible and some almost imperceptible, amply account for the greatest irregularities in the fever-curve.

After the first febrile phenomena have abated somewhat symptoms of respiratory disturbance usually show themselves. A number of small metastatic abscesses may exist without indicating their presence by any symptom, but if they are superficial and are situated near the pleural surface, the patient will generally complain of a sense of oppression and pain at that spot. Symptoms of pleurisy will develop, and auscultation may later reveal an effusion into the pleural cavity, and probably, also, the existence of pneumonia at the base of one or both lungs. With dyspnœa there will be cough with the expectoration of sputa, at first frothy and mucous, later rusty and perhaps purulent. In rare cases only hæmoptysis occurs. Braidwood lays stress upon a peculiar "sweetish," "hay-like" "purulent" odor of the breath, of which he says: "This character of the breath in suppurative fever is very remarkable and of easy recognition."

Metastatic abscesses of the liver cannot readily be recognized unless near the peritoneal covering, in which case localized peritonitis will be indicated by the presence of a sharp pain at that spot. Gussenbauer has recognized the presence of such lesions twice during life by auscultation, a slight crepitus being noticed.

The discoloration of the skin that has gradually developed has now assumed a hue deep enough to be recognized as an *icterus*. It is described by Braidwood as "a yellowish tinge intermixed with the dull leaden or ashy color which accompanies wasting disease." Its origin is not probably due to metastatic inflammation of the liver, which frequently is absent, but is either hæmatogenous or is caused by the presence of micrococcus growths in the capillaries of the skin. The facial expression, though not specially characteristic of the disease, is different from that of septicæmia. The marked emaciation which has already set in gives the eyes a hollow, sunken look. At the same time they show by their anxious expression that the intelligence is as keen as ever, and it may remain so until the final stages of the disease. The dryness of the skin occurring with the initial rise of temperature will be followed by profuse perspiration, a marked symptom as the disease progresses, appearing independently of the chill as well as immediately after it.

Later in the course of the disease erythematous patches are seen, or there is a scarlet rash extending over the greater portion of the body. This rash assumes in pyæmia a most markedly papular or even pustular form, and it is undoubtedly due to colonization of micrococci in the upper layers of the skin. Toward the end purpura spots are seen, and the pustules may coalesce and give rise to foul discharges, or vesicles filled with puriform fluid develop.

There is not found so marked a disturbance of the digestive organs as in septicæmia. At first the bowels may be constipated.

The tongue is furred, the thirst is great, and, as the fatal issue approaches, the tongue becomes dry and brown and is coated at last with a heavy crust, while the gums and teeth are covered with sordes. Occasionally foul and bloody stools occur, but diarrhœa is a more characteristic symptom of septicæmia.

Another marked symptom of pyæmia that develops itself as the disease progresses is *general hyperæsthesia.* The patient complains of a sharp pain, first at one point, then at another. Many of these pains are undoubtedly due to metastatic inflammation, but the general tenderness which manifests itself on the surface of the body cannot be explained in this way. Such patients are extremely difficult to handle or to move about in bed, and if, in addition, there is a severe wound or a compound fracture of the bone, the situation is extremely trying and painful for the nurse as well as for the patient.

Where so much suppuration is going on one would naturally expect enlargement of the glands of the lymphatic system, and with them the spleen; but there is not found that pulpy softening of the spleen which is characteristic of septicæmia. Metastatic abscesses and infarctions may occur in this organ, as elsewhere, in which case there will be an enlargement that can be made out by percussion.

As an indication of the state of the kidneys the condition of the *urine* rarely affords much information. It will, of course, be somewhat scanty and high-colored, particularly at first, and urates may be deposited in excess. A considerable amount of albuminuria with fibrinous casts would indicate a hyperæmia of these organs, possibly due to the presence of metastatic deposits, but possibly also to the febrile disturbance only. Pus-corpuscles are occasionally seen, and at times also bacteria in considerable quantities, due to the effort on the part of the system at elimination of the poison. Hofmeister has accounted for the presence of peptone, which is found in this as well as in certain other diseases, by showing that the active leucocytes in pus possess the power to retain peptone, so that the amount of it can greatly be increased. He regards, therefore, the presence of this substance in the urine as an indication of the breaking down of pus-corpuscles in the body. Hæmaturia has occasionally been noticed, but it is an extremely rare symptom.

Not only are there complications in the internal organs during pyæmia, but on the surface of the body there is also much to occupy the attention of the surgeon. Among the most important of the complications are those found in *joints*. Early in the disease the surgeon may have complaints of pain in the knee or in the shoulder-joints, and an examination of the knee will enable the surgeon to detect readily the presence of an effusion. The surrounding tissues may also be swollen and inflamed for a considerable distance. An incision into such a joint may disclose the presence of turbid serum or pus, which may collect with great rapidity. The sterno-clavicular articulation is often affected, but all joints, small as well as large, are liable to be the seat of inflammation.

Phlegmonous inflammations are also seen, but they more frequently accompany puerperal pyæmia. The surrounding tissues are œdematous and the muscles are of a brawny-red color. Metastatic inflammations of bones are not likely to occur, but in acute osteomyelitis of long bones accompanying some forms of "spontaneous pyæmia" there are signs of most acute and extensive inflammation, accompanied by severe pain. The inflammation of joints may, however, be accompanied by inflammation, and even by suppuration, of the adjacent bones. In amputation-stumps the signs of bone-inflammation are often present. There is an increased discharge of foul pus, and an examination discloses the presence of a sequestrum and of a protruding mass of granulation tissue from the medullary cavity. At a later period "the medulla is found dead, blackened, and encysted, but within it is a putrid mass of bone débris and pus. A probe passes down the entire length of the shaft."

If the *blood* be examined during life, there are found, in addition to the presence of micrococci already mentioned, an increased number of white blood-corpuscles and blood-plaques. The red corpuscles are, however, diminished in number, and many of them have a crenated or shrunken appearance, which may account in a measure for the anæmic pallor of the patient. (See page 100.) Symptoms of heart-lesion are rarely noticed, although in those cases in which ulcerative endocarditis is a prominent feature pain in the region of the heart is occasionally mentioned.

The *pulse* is fairly strong, but is more rapid than usual; in the later stages of the disease its weakness and rapidity are, however, very marked.

The prostration at this period becomes a striking feature, as is also the great emaciation, which at times becomes extreme. All these symptoms will be aggravated greatly by secondary hemorrhages, which are not infrequent, and which are usually hard to control, as they may be repeated even after the ligature of a large vessel.

In the later stages of the disease the mind begins to fail, and there occurs for the first time delirium, which, as the end approaches, gives place to coma. The presence of paralysis, strabismus, sudden deafness, or priapism may point to the existence of metastatic meningeal inflammation. *Subsultus tendinum* will almost always be present.

The usual duration of pyæmia is from ten to fifteen days. Billroth's tables give ten cases which lasted from ten to eighteen weeks. It is probable, he thinks, that the thrombi form in the second week, and are most dangerous from softening in the third and fourth weeks. The writer has seen a case which lasted nearly two months.

The pyæmia which has just been described is that form in which the virus finds an entrance into the system through the surface of a wound. *But it has long been recognized that pyæmia may occur although no wound exists.*

The etiology of this form of pyæmia has already been discussed, and the reader is therefore aware that the micrococci can get into the system by means of an intravascular infection. It remains for the writer merely to mention some of the cases which belong in this category. The most striking, perhaps, of all, and the one which the surgeon is most likely to see, is the case of acute osteomyelitis, generally of the long bones. Such a case is always ushered in by a chill. Symptoms of the most acute inflammation soon show the origin of the fever, and when finally suppuration is established and the abscess breaks, great injury has been done to the bone. A pyæmic complication is not, therefore, to be wondered at when the severity of the affection is considered.

A good many of the cases of ulcerative endocarditis belong in this category, as has been shown. In some the lesion seems to be the primary—that is, the point of entrance of the micrococci into the tissues; in others the endocarditis may be but one of a series of secondary changes starting from an inflamed lung or kidney or from a rheumatic joint. The symptoms will vary considerably according to the disease of which the embolism and metastasis are complications. In the cardiac group, or those which supervene usually in cases of chronic heart disease when weak spots in the shape of fibrous scars exist upon the valves, there will be symptoms of pain in the cardiac region and palpitation, with a sense of distress, and auscultation will disclose a murmur.

In some cases cerebral symptoms seem to predominate from the beginning; suppurative meningitis may coexist with a patch of pneumonia at the apex of one lung and with endocarditis of the mitral valve. Different portions of the body have been examined carefully to find the door through which the virus has entered in these forms of obscure origin. The following case, occurring in the writer's practice, fairly illustrates the type of pyæmia that develops without a wound:

E. I.——, a female thirty-four years of age, entered the medical wards of the hospital with pain in the right lumbar region, which pain had existed for six weeks and which was ushered in with a rigor. She had been in poor health during the winter, and had recently suffered from one or two epileptic seizures. The signs of suppuration growing more marked and pus appearing in the urine, a diagnosis of perinephritic abscess was made, and, as her condition was grave, she was transferred to the writer's wards and the abscess was opened, ten ounces of pus being removed. Chills and increase of fever had developed before the operation. At the time of the evacuation of the pus a gelatin culture was taken, which in a day or two developed into the staphylococcus. No improvement followed; the breathing became labored; involuntary dejections occurred; the pulse ran up to 180, and the patient died on the fifth day after the operation.

At the autopsy there was œdema of the lungs. Miliary abscesses were found on the surface of the heart and in the papillary muscles, and the edges of the aortic valves were thickened. There was hemorrhagic infarction of the spleen and acute purulent nephritis of the right kidney, and miliary abscesses in the central portion of the left kidney had occurred. A small metastatic abscess was found in the intestine, and one the size of a horse-chestnut was found in the liver. A microscopic section of one of the abscesses of the heart showed the typical microscopical appearances, a clump of micrococcus growth occupying the centre. At the demonstration before the class the original aureus culture was shown at the same time with the microscopical sections and the fresh organs in which metastasis had occurred.

In puerperal pyæmia there is pretty much the same chain of events that occur in traumatic pyæmia. According to Baumgarten, the streptococcus is often found in secretions from the vagina, which seems to constitute a sort of lurking-place for it, and the lochia furnish a most admirable culture material. After parturition the uterine contractions, the free flow of the lochia, and the rapid epithelial formations that cover the denuded surface do not give the cocci an opportunity to obtain an entrance. If, however, the contractions are feeble and the lochia are retained, the sinuses are not securely closed, and if epithelial formation is prevented by placental remains, which are very favorable spots for bacterial development, or if the deeper layers of the uterine walls are torn, the door is at once opened to puerperal infection. The form of endometritis which results is usually a diphtheritic one, for the streptococcus has only a feeble peptonizing influence; but during a more prolonged stay in distant parts its capacity to cause inflammation may be strengthened, and it is then fully capable of causing suppuration. It may follow the route of the lymphatics or of the blood-vessels, causing parametritis, ulcerative endocarditis, and metastatic abscess in the various organs. Puerperal pyæmia is said by Billroth to be relatively less malignant than surgical pyæmia. Of a series of 50 cases tabulated by him, 5 recovered, and these 5 were all cases of puerperal pyæmia.

Surgical pyæmia is sometimes divided into acute and chronic forms. The form usually described as chronic is that which has already been studied under the head of Suppurative Fever. The diseases are, however, of quite different character, presenting not only different causes, but different symptoms and pathological changes; they have only this in common: they are both complications arising from a suppurating wound.

As has been seen, pyæmia may kill rapidly in a few days, or it may last weeks or even months. In the latter case the symptoms are not so pronounced as in the acute type: chills are less frequent, as metastatic inflammations are fewer in number. The chances for recovery is such cases are correspondingly greater. Such a case is the following, an example of true chronic pyæmia:

W. C——, twenty-seven years old, a healthy brakeman, received a compound comminuted fracture of the left leg from a car-wheel. Amputation of the thigh was performed through the condyles. Extensive sloughing of the flaps followed, and on the seventh day a hemorrhage occurred from the popliteal artery; the vessel was secured in the wound, but four days later a second hemorrhage occurred, and the femoral was tied at the point of election. Three days later swelling and tenderness of the left parotid showed itself, and eventually an abscess formed, which was opened.

At this date there was also increased respiration with bloody sputa, and at times the patient became delirious. By this time the patient had become anæmic, emaciated, and greatly prostrated in strength. An offensive discharge oozed from the wound. The thigh was shrunken and the wounds were pale and blue. A day or two later a sharp pain in the right side at the level of the fifth rib ushered in a local pleurisy.

Two slight hemorrhages occurred from the point of ligature of the femoral about a month after the patient's entrance to the hospital, and the artery was again tied higher up. He seemed now to be failing; emaciation was extreme, and the sensitiveness of all parts of the body was so great that it was with difficulty that his wounds were dressed. Under stimulants and nourishment he rallied, however, and by the sixtieth day the temperature remained on the normal line for the first time. Pyrexia in a milder form returned later, and on the ninetieth day an abscess formed in the middle of the thigh, although the wounds by this time had nearly healed. After this no further suppuration occurred, and he was discharged from the hospital with two small granulating surfaces at the end of the stump four months from the time of entrance, the temperature having been normal for a week only previous to his departure.

So much has already been said about the pathological changes seen in pyæmia that it would be difficult to give a detailed account of the *post-mortem appearances* without much repetition.

Decomposition in the cadaver does not set in nearly so quickly as in septicæmia. The surface of the wound is of a blackish-green color like gangrenous tissue, the granulations are smooth and glazed, and there is usually little discharge in the wound. Large arteries may be seen occasionally, partly open so far as their walls are concerned, but they are plugged by a protruding clot which is still firmly attached to them. Thrombo-phlebitis exists in veins leading from or adjacent to the wound. The puriform softening may have broken down the entire thrombus, and nothing remains but a soft muddy puriform material, extending sometimes for a long distance beyond all signs of local inflammation.

Excellent examples of thrombosis can be seen in the sinuses after injuries to the bones of the cranium. An examination of the internal organs brings to light the presence chiefly of metastatic abscesses. But it must not be supposed that they are dotted about in the profusion seen in the beautiful anatomical plates of Cruveilhier and others. In the large proportion of a series of cases reported by a committee of the London Pathological Society a post-mortem examination showed the presence of abscesses in the lungs and such a swelling of the spleen and kidneys as one would expect to see in any severe febrile disturbance. The presence of abscesses of the lungs can easily be accounted for, the ramifications of the pulmonary artery being naturally the first lodging-place of a wandering embolus. They are more frequent in the lower lobe, as the branches of the artery are somewhat larger there. They are not usually of large size, but several may run together and form a cavity as large as a hen's egg. Catarrhal pneumonia may surround them. Infarction may also occur. A serous effusion is often found in the pleural cavity; more rarely it is purulent.

The liver is usually in a state of cloudy swelling. Occasionally it is the seat of abscesses, which arise from several sources. They may be the result of thrombosis of the pulmonary veins following abscesses in the lungs, or they may be dependent upon the softening of thrombi in the portal system, or, finally, they may be caused by minute emboli which have passed the lungs. They are supposed to follow, frequently, injuries to the head, and they are not numerous, and frequently are quite superficial. Occasionally a single large abscess will be found in the liver. The liver is said to be, next to the lungs, the most frequent seat of metastatic deposits.

The kidneys are often the seat of miliary abscesses or small emboli (Fig. 27). The metastatic deposits are more frequently seen in the cortical portion, for the reason, as already noted, that the Malpighian bodies are particularly favorable for the lodgment of masses of micrococci. On section, the organ appears swollen and œdematous. The metastatic abscess is the lesion most frequently seen, but infarction may be found also.

Morbid lesions of the heart are not so frequent in the surgical forms of pyæmia as they are in the class of cases that have been described. The mitral or the aortic valve may be affected, but, according to Hutchinson, more frequently it is the mitral, and this author mentions two cases in which the lesion was recognized before death by a mitral murmur. The lesions consisted in nodular growths upon the valves, which subsequently break down and leave the so-called "ulcerations." This process may be so extensive sometimes as to leave an ulcer of considerable size; according to Osler, perforation of the septum has even occurred. Metastatic abscesses may also be found in the muscular substance of the organ. The existence of slight pericarditis may be indicated by the presence of an increased amount of fluid in the pericardium.

The intestinal canal, as already seen, is not so likely to be affected in pyæmia as in septicæmia, and frequently no pathological changes whatever are found. A miliary abscess may, however, occasionally be found in the submucous tissue, and the latter membrane may occasionally also be affected and break down, thus forming ulcerations. The latter may appear as small ulcers penetrating the mucous and vascular coats, and they are occasionally seen near the pyloric orifice of the stomach in puerperal cases. According to Braidwood, the large intestine appears to be more frequently affected, and the ulcers, when of any size, are situated with their long diameters across the axis of the canal.

The brain may be passively hyperæmic, when the heart and lungs are affected, with some effusion in the ventricles. The presence of metastatic abscesses is rare: when seen they are small and are in the cortical portion. One would more likely find patches of congestion in different portions of the brain, or suppurative meningitis. Metastatic deposits have not been found in the spinal cord, perhaps because the lack of well-defined symptoms does not lead to an examination of that organ.

Inflammation of the connective tissue with suppuration is occasionally seen. Gussenbauer has found it more frequent in puerperal pyæmia. Infection may occur through the arterial system, or local metastasis may occur in the neighborhood of the wound, as in one of the cases first reported.

Joint-inflammations are also supposed to be more frequent in puerperal pyæmia, but they are certainly a characteristic also of surgical forms of the disease. The knee and shoulder are the parts most frequently affected, but inflammation is often found in the wrist and in the sterno-clavicular and temporo-maxillary articulations. An inflammation of the latter joint might easily be mistaken for suppurative parotitis. The condition found on opening the joint in the milder form of inflammation is congestion of the synovial membrane accompanied by a more or less abundant effusion of synovial fluid. Later, pus forms, ulceration of the cartilage takes place, and the joint may become completely disorganized. In other cases a large quantity of pus may form in a joint, and on washing it out only very slight traces of morbid action may be observed (Savory). When the joint-inflammation has been severe and acute in type the surrounding tissues are often extensively involved. It is in these cases that the muscles, when cut into, exhibit the brawny condition so often described. Metastatic abscesses are more often found in muscles of the extremities than in those of the breast. Purulent exudation is sometimes found even in the sheaths of the tendons. Bristowe mentions the presence of metastatic abscess in the tongue. Perhaps much of the hyperæsthesia complained of by pyæmic patients may be due to congestions or to inflammations in the soft parts, which at the autopsy escape notice.

The bones are more frequently the seat of inflammation, from which pyæmic poisoning may originate, than the seat of secondary abscesses. The medullary tissues are so constituted, anatomically, as to favor absorption of the products of infective inflammation. The bones in the neighborhood of the wound are likely to show signs of periostitis and osteomyelitis in pyæmic cases. Metastatic abscesses are seen, however, in the diploë of the cranial bones.

The parotid gland is not unfrequently the seat of metastatic abscess. A metastatic panophthalmitis is sometimes caused by an embolism of the retinal and choroidal vessels. Such an inflammation is of course very destructive, and the contents of the globe usually slough and escape. Gamgee has seen metastatic abscess three times in the prostate. Rarer seats of abscess are the thyroid gland, the mediastinum, the testicles, and the ovaries.

The *diagnosis* of pyæmia is not difficult after the disease is well established, for the intermittent type of fever and the chill are sufficiently characteristic, particularly if there be a suppurating wound. The presence of mental disturbance with a sudden chill and fever, and the existence of sloughing tissue in the wound, would be suggestive of septicæmia. If there were considerable digestive disturbance coincident with a chill, the surgeon might suspect the approach of an attack of erysipelas. Emaciation, hyperæsthesia, diaphoresis, and great prostration are symptoms sufficiently characteristic to aid in establishing the diagnosis, which will be confirmed when the existence of a metastatic abscess has been established with certainty.

Speaking of the *prognosis* of pyæmia, Savory graphically says: "Seldom giving any warning of its approach, it will at once convert a case which just before seemed full of promise into one past all hope of recovery; for it cannot be denied that, with rare exceptions, to pronounce a patient the subject of pyæmia is to say that he is a doomed man." Nevertheless, the number of cases of recovery that have been reported is a respectable one. In the first place, there is a relatively high percentage of cures in puerperal pyæmia. In surgical pyæmia most writers report cases of cure. In one case an account has been given of the autopsy performed upon a man who had recovered from pyæmia the year before: the cicatrices of the metastatic abscesses were plainly visible in the internal organs. According to Guérin, these patients do not long survive their recovery.

The *treatment* of pyæmia is of course chiefly preventive. The results obtained by the introduction of the antiseptic treatment of wounds are probably more brilliant than those which the history of any other affection, medical or surgical, can show.

When once the disease is established, it has been suggested that amputation of the injured limb, if the wound be in that region, would cut off the source of the poison. This expedient the writer tried in one case, but without success. At the autopsy it was shown that the puriform softening of the thrombus extended to Poupart's ligament. Still, a number of cases have been reported wherein pyæmia has been arrested by amputation. Ligature of the infected vein has been advised, and more recently opening the vein and removing the infected thrombus.

The investigations of Macewen have given a strong impetus to this mode of dealing with the lateral and sigmoid sinuses in cases of infection following suppuration of the middle ear. As the result of this infection, thrombosis occurs not only in the sinuses mentioned, but the internal jugular vein, especially its upper third, not infrequently also participates in the inflammatory action. When disintegration of the thrombus takes place systemic infection may occur, the emboli lodging themselves in the lungs principally, and occasionally in the liver and kidneys. If an extensive thrombosis has been set up in the sinus, a portion of it may be placed beyond the limits of the infected area, so that while the centre of the thrombus undergoes puriform softening, the extremities may still remain aseptic. As the result of this infection the wall of the sinus may break down and pus may collect between the wall of the vessel and the bone. On opening the bone at the point of the sigmoid groove granulations are often seen covering the sinus, and often along with these there is an oozing of pus.

If the vein-wall is still intact, it may be laid open, and the contents of the sinus may thus be exposed to view, when the disintegrating clot "may be removed by the aid of a small spoon or gently washed out: the former is the safer." In manipulating the contents of the sinuses, especially when removing the thrombus from the side nearest the jugular bulb, care is necessary against admission of air, more especially if aseptic washings be employed. Macewen does not recommend the ligature of a large sinus. Ballance and Horsley have, however, recommended the ligature of the internal jugular in addition to the curetting of the sinus, and this operation may be performed in cases where the infection has extended to this vein. If it is necessary to ligature the vein, it should be done before clearing out the sinus. It must not be forgotten, however, that the internal jugular is not the sole channel between the sigmoid sinus and the lungs.

In the United States the operation of curetting the sinus has been performed successfully by Mixter. About an inch and a half of the sinus was exposed, and, as it showed no pulsation, it was incised and an inch and a half of softened thrombus was removed with an ordinary dressing-forceps. Jack has also performed this operation, without, however, succeeding in saving the patient.

Macewen recommends that infective pustules on the face or lips should be excised and that the main veins should be tied. "In infective wounds of the orbital cavity, rather than permit the formation of infective thrombosis of the cavernous sinus, the serious question of extirpation of the eyeball and clearing out of the contents of the cavity may arise."

The success of this method has been sufficiently great to authorize its employment in other regions of the body, as, for instance, in the femoral vein. It is only radical measures like these that will offer any hope of relief after infective thrombosis has once been established.

Complete disinfection of the wound should of course be attempted if putrefying discharges are retained, and its walls should be curetted thoroughly to remove the layer of germinating bacteria. Metastatic abscesses should promptly be opened and disinfected when possible; and if suppuration is established in a joint, it should not be allowed to go on without an attempt to arrest its progress by surgical interference. Incision and free douching with antiseptics are advised, and in cases of chronic character this procedure may be sufficiently successful to save life.

The administration of antipyretics is not advisable, as most of them have a rather debilitating effect upon the heart. If any drug should be thought desirable to combat the fever, quinine is to be preferred. Alcohol is probably the surgeon's mainstay in the disease, and it should be given freely even to patients who are not accustomed to its use. Their temperate habits will now stand them in good stead. The amount should be so adjusted as not to cause flushing of the face at any time. Easily-digested food of the most nutritious kind should be given with all the care that skilled nursing can devote to its administration.

The hygienic surroundings should of course be considered. If the patient is in a hospital, he may be moved into the open air for several hours a day if the disease is not running too acute a course or the exhaustion caused by the moving is not too great. If the case becomes chronic, a complete change of room and of clothing will often produce the same effect upon the course of the disease that a change of climate does to an invalid.

The weakened condition of the blood should not be overlooked during convalescence. The administration of iron would probably be indicated to repair the damage done to the red blood-corpuscles. It is to be hoped, however, that few surgeons will ever see cases of pyæmia in the future.

XVI. ERYSIPELAS.

ONE of the most frequent of traumatic infective diseases, and one which antisepsis has not yet succeeded in banishing entirely from our hospitals, is erysipelas. It may be defined as an acute inflammation of the skin spreading along the surface, and rarely to the deeper parts, with a tendency to spontaneous recovery. It is accompanied by acute febrile disturbance; it may involve mucous membranes; it may recur. The name is said to owe its origin to ἐρυθρός, red, and πέλλα, skin. There is, however, no good Greek authority for the latter word. Ἐρυσός and πέλας are suggestive words, but have no meaning which would justify their use.

The disease was known to the ancients, but reliable reports of epidemics date back not farther than the latter part of the eighteenth century. Erysipelatous angina was epidemic in Great Britain in 1777 and 1800, and extensive epidemics occurred also in that country in 1821 and in 1832; there was an epidemic in France in 1750. According to Tillmans, during 1843 the disease visited Scotland, Denmark, and Germany, and numerous American authorities bear testimony to the fact that it prevailed in America in 1842. Hall and Dexter give a description of "erysipelatous fever" as it appeared in 1842–43 in the northern section of Vermont and New Hampshire.

The accounts of these epidemics paint pictures of a much severer type of disease than the surgeon is accustomed to see to-day. The inflammation began frequently in the throat. In Indiana the tongue was noticed to become very much swollen, assuming a blackish-brown color, and deglutition was almost impossible. In New England the phlegmonous form was common. One practitioner writes: "The whole surface, under the pectoral muscle extending to the axilla, frequently under the latissimus dorsi running up under the muscles of the shoulder, is, in not a few cases, one extensive abscess." In many cases the muscles and bones were involved, and the discharges were said to be so acrid that the hardest steel was "directly penetrated by it as by nitric acid," and the instruments used in opening an abscess were found, after being laid aside for a few hours, to be entirely unfit for further use. The epidemic prevailed in the greater portion of the Northern States, and large numbers of lives were sacrificed. This appears to have been the last expiring effort of the disease as an epidemic type, for since that time no such accounts are preserved in literature, and during the writer's own experience the disease in that form has practically been unknown.

The origin of the virus of erysipelas has always been a matter of much dispute, many having thought that no specific poison existed, but that the disease was caused by exposure to cold or by meteorological influences. The early experiments made to test the possibility of transmitting the virus to animals, and of thus proving the inoculability of the disease, did not meet with such success as to settle the question definitely. Prominent among these experiments were those of Tillmans, who inoculated rabbits and dogs with virus taken from the large vesicles which form upon the diseased skin, and also with blood, lymph, and pus. Out of 25 experiments conducted in this manner, 5 only were successful. In these 5 cases the disease was subsequently transmitted to other animals. Tillmans concludes that the disease is only mildly contagious, and this was also the opinion of other observers.

Fehleisen, who was one of the first to isolate the streptococcus of erysipelas, succeeded not only in transmitting the disease to animals, but also from man to man. The human inoculations were justified by being used for the purpose of curing chronic forms of ulceration of the skin, such as lupus or rodent ulcer and also sarcoma. Of seven persons thus inoculated, six developed erysipelas; the single failure was probably due to the fact that the patient inoculated had passed through an attack of the disease some three months previously, and was therefore supposed to be protected from a second attack. The period of incubation was found to be from fifteen to sixty-one hours. The coccus was found in the lymphatic vessels of the skin and in the lymph-spaces, and when the culture was pure it never produced suppuration. Fehleisen concludes from his observations that the erysipelas coccus is a specific microbe which will always reproduce the disease when inoculated even in the smallest quantities, differing thus from the staphylococcus, which must be administered in a sufficiently large dose. These experiments upon man were based upon the experience that an attack of erysipelas often exerted a curative effect, but in the cases mentioned the inoculation failed to cure the malignant growths. Finally, a death having occurred from erysipelas in the hands of imitators of this method, further experimentation in this line was very properly abandoned.

The bacteriological studies of Koch, Rosenbach, and other observers fully confirmed those of Fehleisen as to the nature of the organism which is the cause of erysipelas. The single cocci are from 0.3μ to 0.4μ in diameter. They grow in serpentine chains, the links of the chains forming pairs of cocci, as in most forms of streptococci. When each coccus is about to divide it becomes larger and oval, and two cocci result from the fission of the old one. The organism is readily stained with the usual aniline reagents.

The question of the identity of the erysipelas coccus with the streptococcus pyogenes has frequently been raised, and authorities are not yet entirely agreed upon this point. The coccus of erysipelas is somewhat larger than the streptococcus. The culture on the surface of agar appears as a very delicate grayish-white film composed of great numbers of minute colonies closely crowded together. When the gelatin is inoculated fine white granular masses form along the line of puncture, but at the surface there is usually not much growth. The culture shows after twenty-four hours, and reaches its full development in four days. It does not have a solvent action upon the gelatin. The cultures die out at the end of four months.

Baumgarten thinks that the erysipelas coccus and the streptococcus show different degrees of activity in the same species—that they are the same organism, which under different external conditions act differently. The organism when situated in the superficial firm layers of the skin acts with less virulence, causing sero-cellular or fibrinous exudation, while in the loose structures of the subcutaneous tissues it acts more vigorously, causing suppuration. Many modern observers concede that the erysipelas coccus causes not only erysipelas, but also abscess, but many others believe that when suppuration occurs, it is due to pyogenic cocci which have become inoculated secondarily, and that suppuration is therefore merely a complication of the disease. Experimental inoculation with erysipelas cocci has, in the hands of one observer, always produced erysipelas, while inoculations with the streptococcus produced phlegmonous inflammation.

If the organisms are situated in the skin the inflammation will be erysipelatous, but if in the deeper tissues it will be phlegmonous. Tillmans would group all progressive types of inflammation in the same class. Such a classification would place not only cellulitis, but also lymphangitis, malignant œdema, and even fulminating gangrene, in the same group with erysipelas; but our present knowledge of the bacteriology of these affections would hardly authorize such a wholesale grouping.

The cocci are found in the capillary lymphatics of the skin and in the lymph-spaces chiefly, but they are sometimes also seen in the capillary blood-vessels and in the small veins. They may be found even beyond the lines of the inflammation in parts as yet unchanged. Near the red border the growth of organisms is most active. The lymphatics are so crowded with them that leucocytes are hard to find. Chains of cocci may be seen at this point in the adjacent connective tissue, and here also will be observed the signs of active inflammation as indicated by hyperæmia of the vessels, emigration of leucocytes, and swelling of the fibres of the connective tissue. According to Baumgarten, the cocci lie between the leucocytes in the lymphatics, but in the tissues they are occasionally found in the cells. Nearer the centre of the inflamed parts, where the process has been going on longer, the infiltration is greater, but the cocci have, according to Baumgarten, disappeared. They are found in small numbers only in the vesicles. Baumgarten does not agree with Metschnikoff that the disappearance of the cocci is due to phagocytes. The cell-exudation does not take place until after the coccus growth has reached its height, and only a few cocci are found in the cells. The cocci do not spread through the body in the vascular circuit, although they may occasionally be found in the blood-vessels at a distance from the inflammation. The constitutional disturbance accompanying erysipelatous inflammation is undoubtedly due to their presence in the circulation or to the presence of ptomaïnes. The appearance of the disease at a point distant from the seat of the inoculation is clinical proof that the virus may be transmitted through the circulation.

If the erysipelas cocci are identical with some of the chain-like cocci found in decomposing substances, this accounts for the fact that the disease may be acquired both by contagion and by miasmatic infection, as in epidemics; also for its occurrence at certain seasons of the year; and also for Billroth's clinical observations that it is in wounds chiefly discharging decomposing secretion mixed with blood that erysipelas is most likely to occur.

The most frequent *point of entrance* of the virus is through the wound, and from this point it spreads rapidly through the lymph-capillaries of the surrounding skin. In the so-called "cases of idiopathic erysipelas" the disease was supposed to develop itself quite independently of any trauma, but even in these cases it is not difficult to imagine that some minute wound, abrasion, or diseased spot on the surface of the skin may offer a suitable soil for the inoculation of the microbe. The routes taken by the pyogenic cocci in producing boils and carbuncles could readily be followed by the erysipelas coccus. The disease does not always manifest itself at the point of entrance, but it may appear first at some distant portion of the body, thus necessitating transmission of the organism through the circulation. It is possible that the lungs or the digestive tract may allow the passage of the microbe, and that the infection of a certain locality may be through the circulation instead of through the integuments. Whether a slight trauma of the mucous membrane is necessary for such invasion cannot easily be decided. It is, however, highly probable that healthy skin offers a sure protection against infection.

The clinical evidence of the contagiousness of erysipelas is abundant. Fortunately, the material to be obtained on this point belongs to a period that has already passed. The *occurrence of erysipelas following vaccination* has at certain periods become so serious and so frequent a complication that the operation has for the time being been abandoned. This was the case in Boston in the winter and spring of 1850. In the records of the Boston Society for Medical Improvement, Morland, the secretary states:

"Of late, however, cases have multiplied to such an extent, and the result has been so often fatal, that many members of the society have refused to vaccinate except when it has been absolutely necessary, and have almost wholly given up revaccination."

Cabot reported the case of a gentleman sixty-nine years of age who was revaccinated, and at the end of a week phlegmonous erysipelas developed. The disease invaded the chest and the right arm as well as the left. The suppuration was severe about the left shoulder, and the pectoral muscle was thus separated from the parietes of the thorax. Numerous openings were made about the elbow and shoulder for the discharge of pus. The patient was confined to his bed for two months. Bigelow reported a case of a healthy child five months old. On the eighth day there was taken from the vesicle matter with which he vaccinated three other children. On the next day the arm became erysipelatous, and the child died in a few days. All the patients vaccinated from this child had typical vesicles and no anomalous symptoms. Bigelow regarded this as evidence conclusive against the transmission of erysipelas by vaccination.

Tillmans, however, has no doubt that in many cases the vaccine lymph has conveyed the virus of erysipelas. Barbieri vaccinated forty-nine children with virus from a child who had erysipelas at a distance from the vesicle, without his knowledge, and, out of twenty-one children who had a vesicle, twelve contracted erysipelas and four died. This, however, does not prove that the vaccine lymph necessarily contained erysipelas poison, for the points may have become infected after having received the lymph. Whether such a mode of transmission of erysipelas cocci is possible could be determined only by a series of experiments in which all the conditions considered necessary for a reliable bacteriological experiment had been complied with. There is little doubt, however, that inoculation might take place by unclean instruments, so that the pustule might become infected by the virus emanating from a concurrent epidemic of the disease.

The *close relationship of erysipelas and puerperal fever* has long been well recognized, and it is of especial interest in view of the fact, which is now known, that both these diseases are caused by the streptococcus type of bacteria. Dr. O. W. Holmes, in a paper on the contagiousness of puerperal fever, reports an epidemic of that disease in the practice of a physician who made the autopsy in a case of œdema and gangrene of the thigh, and received an injury to his finger which confined him to the house. Several cases of erysipelas occurred in the house where the autopsy was performed, and two of the nurses who cared for the puerperal cases died of erysipelas. Stillé reports the experience of a Philadelphia physician who had 95 cases of puerperal fever in rapid succession, and of the children born in these cases no less than 15 died of erysipelas. But perhaps the most striking example of the close relationship of the two diseases is the following: There was an epidemic of puerperal fever in the Hôpital St. Louis in January and February, 1861: no new cases could be admitted. The puerperal patients already in the hospital were transferred to a dermatological ward, while the patients with disease of the skin—thirty-two in number—were placed in the puerperal ward, whereupon an epidemic of erysipelas broke out among those patients, and several of them died.

The question of the transmission of the disease from case to case has been much discussed, and, although *the contagiousness of erysipelas* has been recognized by many writers, still there are high authorities to-day who are not prepared to accept this view. Gross says: "The question of the contagiousness of this disease is not yet fully settled. Much may be said both against and in favor of this view. My own opinion, founded on considerable experience, is that the affection at times possesses such a character." Stillé says: "But direct clinical proof is also abundant that erysipelas itself is communicable by contagion." The occurrence of several cases of the disease in a certain locality or in a hospital ward is not necessarily evidence of its contagiousness, for such a concurrence of events may be due to a common cause from which each case has taken its origin. But when a case is brought to a given point and it becomes the focus of an epidemic, the evidence in favor of contagion is much more conclusive, as the following examples show:

In 1852 a man arrived in Platte county, Missouri, with facial erysipelas. The farmer who nursed him fell ill with the disease; a second farmer who nursed and slept with these two individuals was taken with erysipelas; subsequently six other persons who helped to nurse these cases were themselves attacked. No other cases occurred in the neighborhood (Stillé).

A young man visited an intern of the Lariboisière in Paris who was ill with erysipelas; on returning to his home in Guise he was taken with the disease, and died in thirteen days. His servant had erysipelas. A relative, who visited him from a distance, two days after his return home was taken ill. His wife also had erysipelas, and likewise three neighbors who visited them during their illness. A relative of the latter who came from a neighboring village to see them was the next victim; also three Sisters of Charity who nursed them, and who, on their return to the convent, infected several other sisters. The physician who attended these cases died of erysipelas, as did also his daughter. Previous to this time there had been no cases of erysipelas in any of these localities.

It was the common experience of many a hospital surgeon, in times past, that a single case of the disease, allowed to remain in the open ward of a hospital, has given rise to no other cases. Such facts as these have caused many to doubt the theory of contagion, and it is highly probable that the average case of erysipelas is but feebly contagious. There are, however, undoubtedly cases which are contagious in the highest degree, particularly when gangrene or phlegmonous inflammations occur as complications. In former times diseases of this type could be followed from bed to bed, and there often existed a certain ward or some bed where the occupants were generally expected to have the disease.

At the present time, when antiseptic dressings isolate a patient so much more effectually from his neighbors, it is probable that a case allowed to remain in a ward where other wounds existed might not communicate the disease. The more complete knowledge of the virus of erysipelas has, however, given rise to greater care to bring about isolation. The old view that the disease may be caused by exposure to cold or by climatic conditions is generally discarded, although these conditions may undoubtedly act as predisposing causes. The season of the year and the state of the atmosphere may at times be more favorable to the development of the erysipelas cocci than at others, and the greater activity of these organisms at certain periods is thus accounted for. Certain it is that in the winter and early spring months this disease is more likely to be epidemic than at other seasons. The presence of decomposing materials provides a soil favorable for the development of the cocci, as has already been seen. The presence of any decaying substance, imperfect drainage, and bad hygienic surroundings are therefore to be regarded as predisposing causes of the disease.

So far as age is concerned, it may be said that in children the disease is comparatively rare. Erysipelas neonatorum is, however, frequently epidemic in badly-arranged lying-in hospitals, and it is usually associated with puerperal fever. This disease does not appear frequently during old age. Whether certain constitutional affections, such as scurvy, alcoholism, diabetes, and tuberculosis, predispose to erysipelas is still a doubtful question. Some individuals have frequent attacks of the disease, and they are supposed to have an hereditary disposition. The idea that persons with a lymphatic constitution, or, as Heuter suggests, those with large lymph-capillaries and broad lymph-spaces in the skin, are more susceptible, is certainly suggestive.

Attention must now be turned to the *symptoms of erysipelas*. When in the course of the healing of a wound there is found a sudden attack of febrile disturbance, ushered in usually with a chill, which has been ascribed by the friends or the attendants to indigestion or to gastric disturbance of some kind, the possibility of an attack of erysipelas should at once suggest itself. Long before any of the characteristic local conditions about the wound are noticed, the presence of prodromal symptoms make themselves manifest. The tongue becomes heavily coated; there is a sense of oppression in the epigastrium, with malaise by day, and possibly with delirium at night. There may also be noticed occasionally some enlargement of the lymphatic glands, particularly those leading from the part, indicating the route through which the absorption of the poison is taking place. A day or two may pass before the local symptoms appear. In the mean time there is no perceptible change in the condition of the wound—certainly not enough to account for the constitutional disturbance. Occasionally there may be an indisposition so slight that the patient is hardly conscious of it, and then the earliest manifestations noticed are in the wound itself.

By far the most characteristic feature of this disease is the *inflammation of the skin*. The local inflammation is recognized by an increased feeling of tension in the wound, with increased heat and usually with an itching or a burning sensation. The erythema often seen about a wound, and caused by hot poultices, by tight stitches, or by other irritating features of the dressing, is easily distinguished from erysipelas, as the former is chiefly hyperæmia, and not accompanied by exudation, and is also limited entirely to the part irritated. Slight pressure will show that there has been no organic change in the tissues. As true erysipelas develops there is diffused redness and swelling more or less uniform in the centre, but at its edges showing a zigzag irregularity of outline that is quite characteristic, one writer having likened it to the burned edges of a sheet of paper. The color is not of that rosy tinge which pure hyperæmia produces, but it has a somewhat more dusky hue. There is mingled with the red a yellowish tinge which becomes more evident on pressure, for then there is noticed a distinct yellowish staining of the skin during the brief moment that the blood is absent from the capillaries. Pressure also shows that there is considerable hardness of the inflamed part; there is usually no perceptible pitting on pressure, except in anatomically loose tissues like the eyelids or the scrotum. There is, in fact, a picture of inflammation, of a very superficial character, of the cutis vera, with an exudation of considerable amount in that structure and in the underlying looser tissues. As the inflammation increases in severity there can be detected with a lens minute vesicles situated here and there or in large numbers. Many of these vesicles run together and form bullæ of considerable size, which are filled first with a clear and slightly yellowish serum that subsequently becomes turbid or at times becomes even purulent. The smaller vesicles soon dry and form yellowish or brownish scabs, so that during the resolution of the inflammation there may be considerable desquamation.

As soon as the local inflammation is once developed it shows a tendency to spread in various directions. The outline continues to be well marked, and, as has been shown, it is strikingly irregular or zigzag, this peculiar appearance being due to the anatomical arrangement of the lymph-channels along which the cocci spread. The general direction of spreading is, when on the extremities, toward the trunk; when on the face, toward the scalp; but at times the route which the disease takes when starting from a wound may vary greatly. It may meander over a great extent of surface. The writer has seen it invade the entire surface of the body. Such forms of erysipelas have been called "wandering" erysipelas (*ambulans* or *migrans*). The disease does not usually remain more than three or four days in any one place: it moves along, involving neighboring parts. Occasionally it may appear at a distant point, and it is then called "metastatic," but this is a form seen chiefly in pyæmic complications of the disease. The parts originally involved may become inflamed a second time after the inflammation has passed on to distant regions. This tendency to recur is quite characteristic of erysipelas. Volkmann says: "It is like a fire over which one has no control; it burns on wherever it finds material, and it suddenly breaks out afresh in a spot where it was supposed to be extinguished."

The duration of the disease is from one to two weeks. It is well to remember that there is always a tendency to recovery. It might even be called a "self-limited" disease. As the inflammation fades away there is an abundant desquamation; the swelling subsides, and, inasmuch as in the ordinary typical cases of erysipelas there is no suppuration, there is a complete return of the skin to its normal condition. But even after the disease has entirely disappeared there may still be a relapse even more severe than the original attack. The writer remembers the case of a lady who had erysipelas during the healing of a wound from amputation of the breast. The attack was severe, but she entirely recovered, and four months later, long after the wound had healed, a second attack occurred, from which she died. There may be repeated recurrences: Pirogoff saw from six to eight such cases, with a fatal termination in one case. Some patients have what is called "habitual erysipelas," coming on at certain periods of the year or occurring always on certain parts of the body. In such a case there is usually considerable permanent thickening of the skin and subcutaneous tissue, giving rise to a condition resembling elephantiasis.

During the progress of the attack there is generally a more or less marked change in the *condition of the wound.* If the healing process has only been going on for a few days in a case of union by first intention, the wound may reopen partially, and its edges will have a grayish, sloughing aspect. The lips of the wound will be swollen, and a thin, serous, purulent fluid will exude. At other times the healing process appears in no wise disturbed during the attack. In open granulating wounds the closing in of the edges may even proceed faster than before, owing to that so-called "curative" or stimulating action which erysipelas exerts. But usually the granulations lose their brilliant color and become dull and glazed, exuding a small amount of thin, sero-purulent fluid. Here and there hemorrhagic extravasations are noticed, and in certain spots the granulations lose their vitality and adhere to the wound as a kind of diphtheritic membrane. In deep wounds which are in the early stages of healing considerable sloughing of the underlying connective tissue may occur, and, if important vessels lie near, there may be some danger of secondary hemorrhage. Such a complication occurred once to the writer after ligature of the popliteal artery for aneurism. The hemorrhage, though quickly stopped by the nurse, was sufficient to prove fatal to a patient already exhausted by the disease. More rarely the wound may be attacked by true hospital gangrene, but such a complication is extremely rare at the present time.

The *constitutional disturbance* which accompanies an attack of erysipelas is usually well marked. The gastric symptoms and the chill have already been alluded to. With the chill there is a rapid rise of temperature, which at times may reach as high as 105° F. With the first onset of the inflammation there is no marked remission of the fever, a slight fall only being noted in the morning. The temperature varies in a most erratic manner, corresponding pretty closely with the local progress of the disease, but the tendency of the fever-curve is to assume the remittent type, and in the later stages this tendency is quite marked (Fig. 74). With

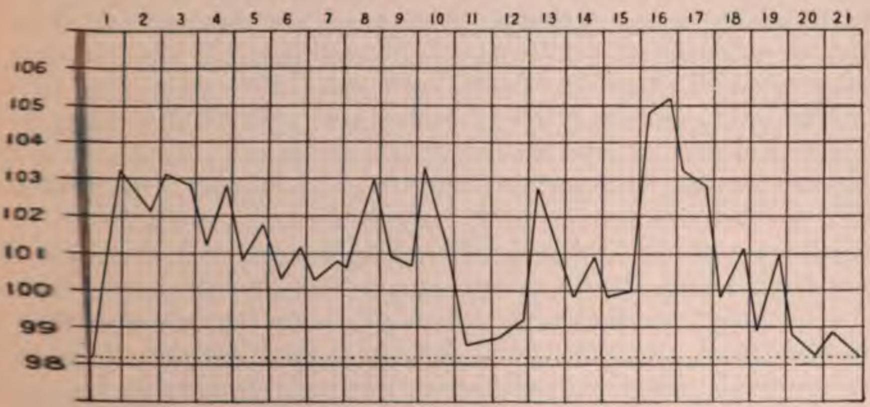

FIG. 74.—Traumatic Fever followed by Erysipelas in a case of Lithotomy.

subsidence of the erysipelas there will be a defervescence with speedy return to the normal temperature, but occasionally the febrile disturbance continues, although the local inflammation has disappeared. There is usually in these cases a considerable rise of temperature in the evening, with a fall to the normal line in the morning. Such cases are apt to experience a recurrence of the local inflammation, and it is the writer's habit to have the patient thoroughly disinfected and removed to a different room, when all febrile disturbance speedily subsides. It has always seemed to the writer that in such cases there took place a sort of auto-inoculation by which the patient was reinfected by the micrococci that had been disseminated through the clothing and the apartment.

After a severe attack of erysipelas the defervescence will often be followed by a subnormal temperature lasting at times for a week or two. There are, however, no other symptoms of collapse, and such a temperature is probably due to the feeble condition in which the patient is left.

The other *varieties* of erysipelas that are usually recognized as such in America are the phlegmonous and the facial.

In the *phlegmonous* variety the disease usually begins, as in the ordinary form, in the skin, and it extends subsequently to the deeper parts. The spreading downward of the process is usually indicated by an increased swelling of the part. The skin becomes more tense and harder. Vesicles and blisters form, which are sometimes filled with a bloody fluid. The surrounding parts are swollen and œdematous. In the mean time the constitutional disturbance is greatly increased, and the fever is more continued in type and at times is of a typhoidal character. The formation of pus may be ushered in by chills, and at the point of suppuration the tense tissue will become soft and more or less fluctuating. A free incision gives vent to a thin and discolored pus in which may be found shreds of sloughing connective tissue. There does not appear to be a circumscribed collection of pus, but rather there is a purulent infiltration of the subcutaneous connective tissue. Large masses of sloughing tissue are eventually discharged, which masses have been likened to wads of wet chamois-leather or to wet blotting-paper. Usually several incisions are necessary to give free drainage to the pus and ichor and the masses of sloughing tissue. In the milder form the inflammation is usually confined to one region of the body, as the leg or the thigh or an arm and forearm. Occasionally, however, the disease assumes a more malignant type. The suppurative process spreads between the muscles, which may be dissected away from the adjacent parts for a considerable distance. The periosteum may be attacked and the bones be laid bare to an extent that gives rise to necrosis. Ashurst, Volkmann, and Gosselin describe a suppurative synovitis which appears to be caused by direct invasion of the joint by erysipelas cocci. The result of such a complication is of course a more or less complete disorganization of the joint, and when more than one joint is involved the termination of the case could hardly be otherwise than fatal. If the synovitis occurs late in the disease, when other symptoms are subsiding, the patient may escape with ankylosis. More frequently it is found in these severe forms of erysipelas that the intensity of the inflammation is expending itself upon the skin, and the disease then assumes the gangrenous type, although occasionally a most extensive burrowing of pus may take place beneath the skin without involving its vitality. Stillé cites such an instance where the skin of the entire abdomen was dissected off the abdominal muscles. When, however, the gangrenous type develops, the kin becomes of a dusky red color which does not disappear on pressre. Large bullæ filled with bloody serum form, which, when disharged, have an offensive odor. At times the skin may become radually pale and white or marbled. The sloughing process will xtend more or less deeply, and fasciæ, muscles, or arteries will be xposed and be involved. At times the gangrene will be limited certain isolated patches of skin whose vitality has been impaired y the violence of the inflammatory process; at other times the angrene will involve large areas and will develop at an early age of the inflammation. The tendency to form pus is slight, nd on incising the parts a foul, discolored serum will ooze from e wound. The constitutional symptoms will become graver at e same time. Such types are most frequently met with in old ibjects enfeebled by disease or by intemperance, or in young chilren affected with tubercle. They are found also in the course of nalignant epidemics such as occurred in 1843 in America.

Some of the malignant types of inflammation associated with lon and palmar abscess are distinctly erysipelatous in their nature, nd are caused by wounds from infected instruments, or they follow juries received during the handling of a cadaver. Medical stunts are occasionally subjected to this affection, and also those ho may come in contact with meat or food in a state of decomsition, as butchers and cooks. The inflammation, starting from slight prick or abrasion on the finger, spreads rapidly up the hand d arm. The lymphatics are usually at first involved, as indicated red streaks extending up the inner side of the arm. The whole nb, however, may become the seat of an acute and rapidly-exnding inflammation. The tendency to suppuration is slight, but he amount of exudation is excessive, and the œdema may spread ven over the shoulder and chest. Although such cases would not be classed by every surgeon in the category of erysipelas, yet Tillmans regards them as such, owing to the tendency of the disease to spread. The conditions found correspond with what one would expect to result from the action of a malignant streptococcus growth —namely, rapid spreading with slight tendency to suppuration. Such cases resemble closely the so-called "malignant œdema" of Pirogoff. As to the *gangrene foudroyante* of Maisonneuve, which is also looked upon by Tillmans as a malignant form of erysipelas, it may be said that there are types of erysipelas where there occurs extensive sloughing of the skin as well as of the parts beneath; but the condition of rapidly spreading gangrene of an entire limb with acute putrefaction, which follows injury to blood-vessels or nerves, can hardly be classed with erysipelas merely because of its tendency to extend itself quickly over a large surface.

The acute inflammations of the fingers and hand, although usually terminating speedily in suppuration, as in felon or in palmar abscess, may occasionally assume a distinctly erysipelatous type. They are accompanied with great pain and constitutional disturbance, the patient usually seeking relief as soon as possible, and they should be promptly dealt with. It is important to remember that a hand or even a life may be saved by active interference.

In the case of a laundress such an inflammation, involving the finger and a portion of the back of the hand, was immediately arrested by free incisions a few hours after the first symptom of trouble had been noticed. No pus escaped, but a turbid serum oozed from the wounds.

Inflammation of the scrotum and penis of a severe type is described arising independently of any urethral complication. The liability of this region to great distention in acute inflammations would make it a favorite seat of the gangrenous type of erysipelas. In other regions, when the tendency to œdema is great, serious complications may result. In a case of erysipelas of the face and neck following a rhinoplastic operation the swelling of the neck was excessive, and pressure upon the glottis produced a dyspnœa that could be relieved only by tracheotomy.

Facial erysipelas has sometimes been called "idiopathic erysipelas," the idea having generally prevailed that this form of the disease was non-traumatic in origin. Although the possibility of an infection through the mucous membrane has already been considered, the opinion has of late years been gaining ground that the majority of cases arise from some slight solution of continuity in the skin itself. It may even happen that at the moment of the breaking out of the disease the little wound may have already iealed, and the erysipelas takes its origin from the germ contained n the freshly-formed cicatrix. The attack is usually ushered in vith a chill which is sometimes of great severity, but the presence f enlarged glands, which may appear before the blush upon the kin, is considered quite characteristic. The most frequent point f departure of the inflammation is the root of the nose. According to Raynaud, the spot where erysipelas first appears is one of he lachrymal ducts, through which the disease emerges from the orresponding nasal fossa, which is endowed with lymphatic vesels emptying themselves into the submaxillary lymphatic glands. 'nder the circumstances one would expect to find the lymphatic lands enlarged and painful.

Starting from the bridge of the nose, the inflammation spreads terally across the cheeks toward the ear, rarely involving the tip f the nose. It is said to have a preference for the right cheek. 'he characteristic irregular outline marks its progress as it gradully spreads over one or both cheeks and finally involves the entire ice. The color is a scarlet-red, tense and shining, shading off nto a darker hue at the ears. The eyelids are the seat of an edematous swelling which completely closes them, and the expreson of the face is so changed as to render the latter unrecognizble. The nostrils are obstructed so that the patient is confined to outh-breathing. The swelling of the ears is also sufficiently great impair the hearing. The chin is rarely involved, this being counted for by the fact that the lymph-stream carries the virus om the upper lip directly to the submaxillary region. The surce of the skin is roughened by the presence of minute vesicles hich may run together and form bullæ whose contents may at times mixed with blood or with pus. The inflammation may involve portion of the neck, but more commonly it invades the scalp, in hich region the color is much less marked, and might be overoked when the hair is abundant. There is, however, considerable elling, pressure is painful, and the glands at the back of the neck e enlarged and sensitive to the touch.

An aggravated form of the disease will be accompanied with a gh temperature which is more or less characteristic. During the rly stages of the inflammation the pyrexia will be of the conued type with slight evening exacerbations, the temperature rying from 103° to 104° F. At the end of four or five days there ill be a defervescence which is usually quite rapid. Before the mperature becomes normal, however, there will be one or more exacerbations which are caused by local outbreaks of erysipelas. During the height of the fever there is, in most cases of this variety, more or less delirium, which is explained in the majority of cases by an irritation of the cortical substance of the brain due to reflex nerve-action or disturbance of the vaso-motor system, or by the sepsis which causes the fever. The extension of the disease to the scalp is accompanied by an aggravation of the brain symptoms, but it is rare that any pathological changes are found in the brain or its meninges to account for them. Suppurative meningitis, when it exists, is usually caused by direct extension of the erysipelas into the orbit—a locality where abscess may occur—and thence by a continuation of the suppurative process to the membranes through the orbital fissure. The delirium, therefore, is not necessarily a dangerous symptom, and ordinarily it disappears with the subsidence of the fever.

The tendency of the inflammation to involve the tissues of the orbit is a characteristic symptom of the graver form of facial erysipelas. The distention of the eyelids is so great as to cause, in rare cases, gangrene. Considerable disturbance of vision may be caused by conjunctivitis, by congestion of the sclerotic, by cloudiness of the cornea, and by œdema in the orbit, but the latter symptom will disappear with the subsidence of the inflammation. If there is deep-seated pain and protrusion of the eyeball, with disturbed or complete loss of vision, an extension of the erysipelas to the eye itself may be feared. Blindness, which is occasionally seen as the result of facial erysipelas, is caused by atrophic degeneration of the optic papilla or by panophthalmitis with suppuration and destruction of the eye itself.

Erysipelas neonatorum, which is a very fatal malady, is rarely observed outside of hospitals. The close connection between this disease and puerperal fever has already been alluded to. The period at which it is most frequently seen is at the time of separation of the umbilical cord, and it is from the granulating surface of the stump that it takes its origin. At first there is but little fever, and the slight blush about the navel or the pubes is often regarded as an unimportant symptom. The skin, however, soon becomes a brighter red, and the subcutaneous cellular tissue is indurated and swollen. The next day the inflammation has spread to the genitals and the thighs, below and over the abdomen. The constitutional symptoms now become strongly marked: there is high fever with great prostration; the child cries, and there is great restlessness. The skin in the later stages may become gangrenous, or phlegmonous inflammation may occur. Finally, the patient falls into a state of collapse, and succumbs to the disease on the sixth or the tenth day. Inflammation of the tissues and the navel is well marked. There may be found both periarteritis and periphlebitis. The tendency of the arteries to become involved is due to the great thickness of the periadventitial tissue, which is nearly double that seen in the veins. The inflammation extends to the point at which the hypogastric arteries are reflected upon the walls of the bladder. When phlebitis occurs, it will extend along the walls of the veins and into the liver. Pus may be found in the surrounding cellular tissue, and peritonitis may also be a complication, and even the pleura may be affected. A peculiar sclerosis of the cellular tissue of the affected parts has been described, particularly of the lower extremities and the pubes. Patches of brown and discolored skin mark the seat of this lesion, but the question whether this affection is to be regarded as a complication of genuine erysipelas is considered by Tillmans as doubtful.

Erysipelas is found not only in the skin, but occasionally also in the *mucous membranes*. Attention has already been called to the fact that nasal erysipelas is one of the most frequent points of departure of facial erysipelas. Raynaud states that the advent of the latter affection may be foretold by the swelling of the lachrymal duct caused by the passage of the inflammation through that canal. When the pharynx is involved there is seen in the beginning a marked enlargement of the submaxillary and cervical glands. There is a burning sensation in the throat, with dryness and a tendency to dyspnœa or difficulty in swallowing. The color of the throat is a dark red, diffused or in patches, and the swelling is considerable, involving more or less the tonsils. Later, vesicles form, which vesicles soon break and evacuate a serous or sero-purulent liquid, leaving behind little yellowish-white patches which are easily removed. The disease lasts five or six days. Occasionally the throat may become the seat of a gangrenous or diphtheritic inflammation, or there may form an abscess somewhat similar to the retropharyngeal abscess. In some cases there is an extension of the inflammation to the mouth, the tongue in this event becoming more or less swollen. In malignant epidemics, such as that described as occurring in 1842 in America, the enormous swelling of this organ gave rise to the name given to the epidemic itself—"black tongue."

The inflammation may make its way from the pharynx through the Eustachian tube to the external auditory canal and thence to the head and scalp. The mucous-membrane inflammation may also be secondary to the facial erysipelas, the disease finding its way in through the mouth, nose, lachrymal duct, or auditory canal.

The disease does not stop at the pharynx, but may extend down as far as the glottis; it usually stops here, and only occasionally extends and gives rise to œdema of the glottis. Such a complication is of course nearly always fatal. Finally, the inflammation may be traced as far as the lungs, in which case all the symptoms of pneumonia may develop. Trousseau described erysipelatous pneumonia, or pneumonia migrans, which differs from the common form in not involving an entire lobe, but, beginning insidiously and involving a circumscribed area, it moves from place to place, an apparent resolution taking place in the parts successively involved, until the entire lung becomes affected, and even double pneumonia may result. This form runs its course slowly, and there are frequent improvements with relapses. Raynaud does not accept the identity of this form with true erysipelas unless a distinct extension of the disease from the skin or the mucous membrane has taken place. Without a coexisting erysipelas it would not be justifiable to make such a diagnosis.

That erysipelas may involve the female genitals has already been shown. The rectum is occasionally also the seat of the disease by extension from the nates. The writer had an opportunity of observing this form in a case of cancer of the rectum, the disease breaking out after a digital examination. Both nates were extensively involved. Complete relief of the symptoms of stricture followed, and an examination later showed that the cancerous mass had disappeared. Unfortunately, there was eventually a return of the carcinoma.

The principal *anatomical seat of the disease* is in the skin. If this organ be examined, the cells of the epidermic layer will be found much swollen or raised up by fluid in the form of blisters. The cells of the rete are enlarged and swollen, and there is a serous infiltration of the lining membrane of the hair-follicles and the sweat-glands. In the upper layers of the true skin there is a rich capillary network of lymphatic vessels, and this region is the principal seat of the coccus growth. The cocci are seen crowding these capillaries and spreading also into the connective-tissue spaces. The bacteria are most numerous near the margins of the erysipelatous blush. In the neighboring parts, which have not yet been attacked, cocci are more or less numerous in the lymphatics of the skin, and even in the subcutaneous tissue. Near the red border they have already reached their highest degree of development. The lymphatics are so crowded here with cocci that the leucocytes are not visible. The cocci may also be found between the bundles of connective-tissue fibres. Within the border-line there are greater hyperæmia and exudation of leucocytes, which are seen emigrating from the blood-vessels in large numbers. Proliferation of the cells of the connective tissue is also going on, but these cells do not appear to take any active part in the process. Nearer the centre of the diseased area the cocci are no longer to be seen, but the inflammatory exudation has reached its highest point. The vesicles on the surface are filled with a turbid serum, but the cocci are seen here only in small numbers. When the growth of the cocci is unusually active the surrounding tissue undergoes necrosis and minute abscesses may form. Undoubtedly many such abscesses develop, and they are subsequently absorbed without any external indication of their presence. In the more malignant types of erysipelas suppuration occurs on a larger scale, and it is probable that this process is due to the activity of the erysipelas cocci, which occasionally seem to possess true pyogenic qualities. After an active growth in various directions the organisms cease to continue their development, and the further progress of the disease is thus arrested.

The micrococci are not found in the capillary *blood-vessels* of the part affected. That a certain number of them find their way into the circulation has been abundantly proved. The reason why metastatic foci of inflammation are not thus established is to be found in the fact that after leaving the original seat of their development the organisms are speedily destroyed.

Masses of micrococci are occasionally found in distant organs and in the enlarged glands. Although bacteria are found in the blood only in small numbers, the peculiar changes seen in the blood-corpuscles have been attributed by Heuter and others to the presence of the micro-organisms. The precise reason for these changes is not yet clear. The red blood-disks assume a peculiar crenated appearance. They not only shrink, but readily dissolve and run together, looking, as Stillé says, like streams of yellow fluid crossing the microscope. Fatal hemorrhages occurring during the progress of the disease have been ascribed to this condition of the blood. The white corpuscles are usually increased in number. Endocarditis may occur, involving the bicuspid and mitral valves, and also pericarditis. A slight systolic murmur is frequently heard, which usually disappears with the erysipelas.

The condition of the heart-action may largely be due to the state of the blood and to some fatty degeneration of the muscular tissue. Fatty degeneration of the diaphragm is sometimes also noticed.

The *gastric disturbance* so characteristic of this disease is not explained by any well-marked local changes. It is probably due to the general septic condition of the system. Ulcerations of the small intestines, such as are seen following extensive burns, are occasionally found. They are probably of catarrhal origin, and may be the cause of the bloody diarrhœa which is occasionally observed.

The *cerebral symptoms* which occur in facial erysipelas would lead one to expect marked changes within the cranial cavity; but this is not the case. The brain and the membranes may be somewhat hyperæmic and œdematous, and the large sinuses and the veins may be filled with dark serous blood and thrombi in a limited number of cases. Suppurative meningitis, which is extremely rare, results from the invasion of a phlegmonous inflammation through the orbit.

Among the other material changes may be noted enlargement of the spleen, parotitis, and cloudy swelling of the kidneys. Neuritis may be found in rare cases in the nerves of the parts affected, which affection may give rise to muscular contractions. In grave cases, when pyæmic infection has become a complication, there may of course be found the numerous pathological changes resulting from sepsis.

The *curative influence* of erysipelas when it occurs in the course of other chronic diseases has already been mentioned. Occasionally the wound itself will seem to heal more rapidly, and the granulations to have a more ruddy and vigorous appearance than existed previous to the attack. Chronic inflammations of the skin, particularly those of a tuberculous or syphilitic character, have been known to yield to an attack of erysipelas that resisted all kinds of treatment. Volkmann, Grivet, and others report quite a number of cases of lupus permanently cured in this way. Chronic ulcers of the leg have been stimulated to heal, and also old sinuses connecting with joints or bones. The therapeutic use of the products of the organism will be discussed elsewhere. (See Appendix.)

Raynaud reports, in Ricord's clinic, a case of phagædenic chancre which for two years resisted all kinds of treatment. Finally, Ricord suggested that an attempt be made to bring on erysipelas. All kinds of irritating dressings were tried in vain, as well as charpie saturated with pus. Two months later, erysipelas appeared spontaneously, and the chancre was healed in a few days.

Old neuralgias often improve after an attack of erysipelas, and likewise in the insane a temporary improvement has been observed. The disappearance of tumors has been frequently noticed. The writer has already called attention to a case of cancer of the rectum in which the growth melted away before an attack of erysipelas. Tillmans and Coley have collected a number of cases of sarcoma cured in this way. (See Sarcoma.)

A woman forty-three years old, having a sarcoma the size of an apple on the left cheek and two other sarcomatous nodules on the face, was operated upon by W. Busch for the removal of a lobe of the larger tumor. Two days later erysipelas appeared and considerably diminished the size of the tumors; after a relapse they disappeared entirely.

A man twenty-eight years of age, having a large incurable lympho-sarcoma of the left side of the neck extending from clavicle to parotid, after entering the hospital had facial erysipelas which involved the neck. During the illness, which lasted eight days, the growth diminished one-half in size. Two days later the patient died, and at the autopsy an extensive fatty degeneration of the cells of the tumor was observed.

The observation made in the latter case probably explains the process by which absorption takes place. The feebly resisting power of the diseased cells renders them less able to resist the action of the micro-organism. It must not, however, be supposed that erysipelas always has this effect upon morbid growths on the surface of the body. The writer has more than once seen epithelial ulcers of the face which had passed through an attack of the disease with their vitality unimpaired.

The *diagnosis* of erysipelas is usually not difficult when the inflammation of the skin is fully developed. In the early stages, however, before the local symptoms appear, there is no sure guide. Gastric symptoms with febrile disturbance which cannot be accounted for after careful examination of the patient strongly suggest the near approach of erysipelas. Enlargement of the glands adjacent to the part affected is usually alluded to as an important sign, but it would not, in the writer's opinion, be wise to rely upon a mere enlargement unless the swelling be manifestly acute and be accompanied with indications of an adjacent skin-inflammation.

The erysipelatous blush is sufficiently characteristic. The doughy swelling of the skin, the yellow infiltration, and the peculiar zigzag outline slightly raised above the level of the adjacent healthy skin are all sufficiently constant to avoid confusion with erythema, with inflammation due to abscess in the wound, or with irritation from tight stitches. In abscess there should be a rise of temperature, but in the other conditions the constitutional disturbance would probably be so slight as to show clearly their nature. There may be some difficulty in recognizing erysipelas in certain regions, as in the scalp. The presence of inflammation on the face or the ears, together with enlargement of the occipital glands, will then help to establish the diagnosis.

The difference between phlegmonous cellulitis and phlegmonous erysipelas is one which in some countries is not recognized at all, and in general it is regarded difficult to distinguish between them. The cellulitis usually starts from a severe wound, owing to the failure of antisepsis in the early stages of the healing process. The most frequent example is that accompanying compound fracture. The inflammation in this case is essentially deep-seated, and the skin is not the seat of a distinct and independent inflammation, but it is involved only to such an extent as could be accounted for by the inflammation of the deeper-seated cellular tissues. The appearance of the suppurating tissues shows less tendency to gangrene in cellulitis than in erysipelas.

The *prognosis* of erysipelas is, on the whole, favorable. After a few days of inflammation there is a marked tendency to resolution. The experience of different surgeons and physicians, however, varies greatly. Stillé never met with a fatal case of facial erysipelas where supporting or palliative treatment had been tried. He had, however, seen it fatal when evacuant, sedative, or alterative measures had been employed. Trousseau and Chomel, both of whom had a large experience in medical erysipelas, had hardly ever seen a fatal case of the disease. Gosselin, however, had a mortality of 20 per cent. in facial erysipelas. In surgical erysipelas it was as high as 43 per cent. This is certainly an unfavorable showing—far more so than the experience of the majority of surgeons of to-day would give. The sanitary surroundings of the hospital patient were probably far inferior to what they are at present, and it is possible that many of these cases may have occurred during the period of an epidemic, which always exerts an unfavorable influence upon the prognosis of the disease.

The nature of the wound is supposed to be a factor in the question of mortality. Large or fresh wounds are considered as more likely to be followed by graver forms of the disease than small or granulating wounds. If the disease attacks the mucous membrane, as in the throat, it will probably be severe; if the vagina is the point of origin, as in puerperal cases, there may be reason to fear pyæmia or septicæmia. The deeper-seated types of the disease, such as the phlegmonous or the gangrenous, have undoubtedly a higher mortality than the cutaneous forms.

In individuals enfeebled by long-standing suppuration, and in alcoholic subjects, the disease will prove a formidable complication. The same may be said of a number of organic diseases, such as diabetes and Bright's disease. For similar reasons youth and old age are periods of life when the patient is less resistant to its influences than when in the prime of life.

Velpeau said that the disease was not dangerous in itself, but only through its complications, and in this opinion the writer's experience would lead him to agree. Secondary hemorrhage and œdema glottidis have led to a fatal termination in two cases which might otherwise have recovered. Even a mild form of the disease, without complications of any kind, may carry off an aged person. As a rule, however, it may be said that erysipelas is in the large majority of cases a mild disease, and one which has a strong tendency to get well of itself, quite independently of treatment. The writer's experience of fatal cases has been exceedingly small, and since the antiseptic system has been so highly perfected in all its details, the cases that do occur seem to run a milder course. At the present time the hospital surgeon has only to dread those cases which are imported into the hospitals, and which occur usually in neglected and enfeebled subjects. The cases of facial erysipelas which the writer has met with in private practice have nearly always been severe. The fever, the facial deformity, and the cerebral symptoms make a formidable group. The writer does not remember, however, to have seen but one fatal case.

The *treatment* of erysipelas may be divided into local and constitutional. Of the latter form there has always existed two principal varieties, which, in general, may be divided into supporting and depletive. Depletion is an inheritance from ancient times, when venesection, emetics, and purgatives were the fashion. The object of bloodletting, and the reason that it at one time became a more or less popular treatment in the disease, was the effect produced upon the circulation of the brain and the consequent relief given to cerebral symptoms. It may have acted also as a ready method of eliminating the virus from the system, although the number of cocci found in the circulation is not sufficiently large, so far as our knowledge at present goes, to enable one to say that they would be removed in any considerable number in this way. It can be conceived that occasionally the conditions existing in a particular case would justify venesection. In a case of facial erysipelas in a plethoric individual with violent delirium a resort to this mode of treatment might be justifiable, but the surgeon should hesitate to advise it in other than exceptional cases. Apart from the possible infection at the point of puncture, and the possibility of the formation of a septic thrombus, the danger of lowering the vitality in a disease which not infrequently has a typhoidal tendency is not lightly to be regarded.

Emetics are now so rarely given for any disease that it seems hardly necessary to say a word about them. They may, however, be classed with cathartics as a method of eliminating the virus, for it is probable that the only benefit that could be derived from a cathartic would be this. A laxative might be given at the outset if there is reason to believe the bowels are overloaded. Caution should be observed in this disease to avoid any form of treatment that would act in a depressing way upon the system, and, as a rule, it would be prudent, therefore, not to adopt any of the measures which have just been alluded to.

A great variety of internal remedies have been suggested that were supposed to possess special virtues in this affection, the most prominent of these being iron. By English writers iron has at times been regarded as almost specific in its action. It was first recommended by Hamilton Bell, who gave 25 drops of the tincture of the chloride of iron every two hours day and night. The theory of the action of iron is probably based upon the influence which the cocci are supposed to have upon the red corpuscles. The readiness with which they assume a crenated or shrunken appearance has been ascribed to the loss of hæmoglobin removed from them. Iron is also supposed by Stillé to have a constricting action upon the blood-vessels.

A large number of English writers endorsed the treatment of Bell, but in all the latest publications the writer finds the statement of Pick quoted, that, although he has used it in drachm doses every two hours, he has failed to obtain any benefit from it. In the writer's experience iron has not seemed to have exerted any special action upon the disease, although he has not given it in so frequent doses as is advised by the English school. Iron has received endorsement from other nations as well as England, both French and German writers having used it with satisfactory results. Stillé also gives the drug his endorsement, although he believes the measure of its utility is not always the same. It seems to him best adapted to the less sthenic forms of the disease or to those cases where marked debility is present. Cerebral symptoms do not appear to contraindicate its use.

Pirogoff strongly recommends camphor: he finds immediate results on the use of frequent doses during the first twenty-four hours. It is said not only to diminish the fever, bringing on a profuse perspiration, but also to lessen the delirium. It must not be used continuously for any length of time, as "camphor delirium" may be produced. Digitalis and aconite are among the remedies that have had their day in the treatment of this disease. The drug used perhaps more frequently than any other is quinine. It has been supposed to exert an action on the cocci through its power to arrest the migration of the white corpuscles. But as this does not afford an adequate explanation, it has been supposed also to act in virtue of its antipyretic power. According to Stillé, it seems to act as well in small and moderate doses as in large antipyretic doses. The writer is in the habit of omitting it when the cerebral symptoms are urgent, but he gives it usually in 5- to 10-grain doses, in combination with iron, three or four times a day. Its tonic action gives it a decided advantage over many other drugs.

"The use of alcoholic stimulants in ordinary cases of the disease is not only unnecessary, but injurious," according to Stillé. Tillmans, however, recommends the administration of alcohol as a most valuable remedy both as a stimulant and as an antipyretic, and he is in the habit of prescribing a mixture of sherry with champagne. Under the action of the alcohol, he thinks, with suitable nourishment, one sees the disappearance of cerebral symptoms. Pick advises the use of stimulants in almost all cases, even from the commencement, and occasionally in large quantities.

In the milder forms of erysipelas it is the writer's habit to rely chiefly upon food to preserve the patient's strength. In old or feeble subjects, in the typhoidal types of the disease, or in cases when the amount of nourishment is insufficient from any cause, alcohol is clearly indicated. It is important to remember that delirium does not necessarily contraindicate its use, and that, on the contrary, in many cases nervous disturbance may disappear as the action of alcohol upon the system begins to be felt. Should it be necessary to use other measures to keep the patient quiet, the bromides, chloral, and even opium, can be employed without danger. The antipyretics have but little influence upon the course of the fever, as their action is but temporary, and they do not belong to the class of drugs which would be used appropriately in a supporting treatment.

There is hardly any disease upon which such a vast array of salves and lotions have been expended as erysipelas. In the writer's student days, when erysipelas was the constant companion of the hospital patient, local applications were confined chiefly to the margin of the blush, the adjacent healthy skin being painted with a narrow stripe of nitrate of silver to prevent the further progress of the inflammation. Fresh applications were made as the disease crossed the line thus drawn. Tincture of iodine was used in the same way, but it was also painted extensively over the inflamed surface, and it probably exercised an antiseptic action upon the micro-organisms in the skin. As a local application carbolic acid is probably used at the present time more than any other drug. White thinks that he can obtain absolute control over the disease by an application of an evaporating lotion of ½ drachm of crystallized carbolic acid to 4 ounces each of alcohol and water, the part being kept wet with this solution either constantly or on alternate hours during the day and evening. The disease should yield to this treatment within forty-eight hours.

Heuter first recommended subcutaneous injections of carbolic acid in 2 per cent. or 3 per cent. solutions. The injection should be made near the border of the diseased part, and about two Pravaz syringefuls should be used at one time, the dose being repeated at intervals of one or two days. The material injected should be spread over as great a surface as possible by passing the point of the needle in various directions. This precaution is taken to avoid abscesses, which have been observed to form at the point of puncture. The number of doses is subsequently increased to four or five daily. The erysipelas usually spreads over the first points of injection, but it is arrested on the third or the fourth day.

A simple and comfortable way to apply carbolic acid is with liquid vaseline as a vehicle. It can be painted on the diseased surface with a soft brush. If a considerable area is to be covered, it would not be advisable to use a stronger solution than 1 per cent. In the early stages, when a small patch of the disease exists, a 5 per cent. solution may be used to advantage. The part can be protected by covering the vaseline with a film of gutta-percha tissue or with oiled paper. Whatever way the drug be used, it is hardly necessary to say that in the earliest period of the disease the treatment is likely to be far more effective. This rule applies with especial force to subcutaneous injections.

Carbolic acid in a mild form can be brought to bear upon the disease through the agency of the class of preparations to which belong creolin and phenyl. These preparations can be applied in a strength of 2 per cent. on hot poultices of cotton or other material. Such a method is well adapted to erysipelas of an extremity. The treatment can be made more effective by holding the hand or the foot for an hour thrice daily in a hot bath of the same solution. The advantage of these preparations is that they are not liable to cause carbolic-acid poisoning—a complication which should always be kept steadfastly in mind when applying this drug over large surfaces. Concentrated solutions of salicylic acid have been injected subcutaneously around the borders of the diseased tissues, and a solution of sulphocarbolate of soda has also been used in the same way.

The discomfort caused by the swelling of the skin is greatly relieved by any soothing material which can be so applied as to exclude the air. Dusting on starch or burnt flour accomplishes this exclusion, but it is soon brushed off or is caked up into dry masses. The frequent application of oil or of vaseline to the face with a soft camel's-hair brush relieves the sensation of burning and stiffness, and it is generally a very soothing remedy. White paint has been used in the same way. A drug which involves the adjustment of a dressing to the face is much less agreeable to the patient. Frequent changes of temperature should be avoided, and exposure to cold, it is needless to say, is liable to aggravate the symptoms of inflammation.

The treatment of the wound, if there is one, should vary greatly according to the changes which have taken place in it. Occasionally no change of dressing will be necessary, but if there is much sloughing of connective tissue, free drainage must be secured and appropriate antiseptic remedies must be supplied. In phlegmonous erysipelas, it is important to recognize pus as early as possible, and to give it free drainage by multiple incisions if necessary. It is in these cases that prompt surgical interference may be productive of the best results. The tendency of the poison to spread along the loose connective-tissue spaces must be checked promptly, no matter how long or how numerous the incisions. Very hot and large antiseptic poultices are now indicated, and they should be changed several times a day, combined, if necessary, with antiseptic baths, as every opportunity should be offered for a discharge of the sloughing tissues. The graver forms of gangrenous erysipelas or malignant œdema must be dealt with promptly and heroically by long and deep incisions. Many a life has been saved by the prompt interference of the surgeon. Small incisions, under these circumstances, are worse than useless.

In phlegmonous erysipelas of the face pus forms in the orbital fat, necessitating an incision between the eye and the orbital margin. In scrotal erysipelas of a phlegmonous or a gangrenous character a free incision should be made through the raphé, completely dividing all the tissues involved. This incision usually results in a prompt arrest of the inflammatory process, and the wound heals rapidly.

In the treatment of erysipelas of the mouth, the nose, and the fauces the practitioner must be guided by the general principles that govern the antiseptic treatment of septic inflammations of that region. Applied in the form of spray, antiseptic drugs may not only control the activity of the coccus, but they may help also to ward off the complications that may arise from œdematous swelling.

In the vagina iodoform powder may be used freely, and antiseptic douches should frequently be given.

As soon as the diagnosis of the disease has been made the patient should be removed from a ward containing other cases, and complete isolation of the case should be preserved. This point should be strongly insisted upon, as, until very recently, erysipelas has not been regarded as a contagious disease. The thorough demonstration of its bacterial origin ought at the present time to leave no doubt in any reasonable mind upon this point. It is important also to realize that with the desquamation, which sets in early, the apartment is soon filled with the germs of the disease, and that thorough ventilation and frequent change of clothing and sheets are therefore matters to receive especial attention. The tendency to relapse, so characteristic a feature of the disease, may find its explanation in the infection of the wound from the patient's own surroundings. The writer has not infrequently seen a chronic and relapsing type of the disease arrested, or a tendency to undue prolongation of the pyrexia cut short, by removing the patient to another room. During the period of convalescence the treatment should be tonic and supporting, and care should be taken to avoid exposure to cold, to draughts, or to fatigue. So long as desquamation lasts isolation should be continued, and in private practice the patient should not be allowed to mingle freely with other members of the household, especially during periods of epidemics, until it is tolerably certain that the diseased organisms have been eliminated from the system.

XVII. HOSPITAL GANGRENE.

THE task devolving upon the writer in this chapter is one of unusual difficulty, for the disease to be considered is one with which few teachers of to-day have had experience and which students never see. The impress of the antiseptic treatment of wounds having been sufficiently strong to stamp out, at least for the present time, one of the most baneful of the traumatic infectious diseases, hospital gangrene has become a historic disease.

It is not improbable, however, that many students of to-day may be brought in contact with it, for, although the discipline of hospital surgery has banished the disease from the wards, it is possible that cases may be brought into hospitals for treatment in the future, as they have in time past, or, what is more probable, that the disease may be met with in private practice. Paradoxical as it may seem, it is nevertheless true that hospital gangrene during the past decade has been seen only in private practice. As complete a disappearance of the disease has, however, been reported in former times, and it is highly probable that the occurrence of war, of great epidemics, or of any disaster which may profoundly affect the present well-regulated system of hospital service or of surgical aid to the sick poor in large centres of population, will bring back this unwelcome guest.

Hospital gangrene is a contagious traumatic disease characterized by a diphtheritic wound-inflammation produced by a poison the precise nature of which is not yet fully understood, and it is usually accompanied by more or less profound septic constitutional disturbance. It has been known from the earliest times under various suggestive names, such as "wound-typhus," "wound-cholera," "pourriture d'hôpital," "sloughing phagædena," "nosocomial gangrene," etc. One of the earliest descriptions of the disease is by Pouteau in 1783. He describes it as *une maladie qui jusqu' à present n'a occupé la plume de personne.* The most classic clinical descriptions of the disease were given by Dussaussoy in the latter part of the last century, and by Delpech in 1815, based, as they must have been, on an experience which could have been obtained only under the peculiar conditions of that historical period. Indeed, "history" and gangrene may be said to be coeval, and it is to the medical reports following great wars during the present century that surgeons are indebted for the most valuable data bearing upon the etiology and the treatment of the disease. Crowding of hospitals alone does not appear to be a sufficient cause, but when overcrowding follows the infliction of great privation and fatigue, the conditions most favorable for an outbreak of the disease seem to be obtained. A brief reference to some of the campaigns of late years will illustrate these conditions. With Napoleon in Egypt the disease was reported as very fatal. According to Macleod, in the English army in the Crimean War the development of hospital gangrene resulted from the lowered general health rather than from specific causes. "It was in many cases a veritable child of the typhus." The French suffered much more severely than did the English. "The system they pursued of removing their wounded and operated cases from the camp to Constantinople at a very early date, the pernicious character of the transit, the crowding of their ships and hospitals, all tended to produce the disease and render it fatal when produced." Many of their cases commenced in camp. On one of their transports sixty bodies were thrown overboard during the short passage of thirty-eight hours to the Bosphorus. The disease raged in the hospitals on the Bosphorus, and followed the returning wounded soldiers even to the hospitals in the south of France. "Both in the French and in the Russian hospitals gangrene was often combined with typhus, and in such cases the mortality was fearful." Men who had been wounded after unusual exertion seemed more susceptible to the disease. Macleod states that after the assault on the Redan not a few cases of amputation of the thigh were lost from gangrene of a most rapid and fatal form. In the camp at Scutari the wounds generally assumed an unhealthy aspect when the dreaded sirocco prevailed.

During the Civil War the total number of cases reported by the Surgeon-General was twenty-six hundred and forty-two. The conditions under which some of the epidemics occurred are very suggestive. Keen reports one of the earliest which took place in 1862 in Frederick, Maryland, after the battle of Antietam. He says: "The old general hospital, which had contained six hundred beds, was so crowded with patients that one thousand were of necessity placed in the wards, and one thousand eight hundred men were fed at tables and slept somewhere." About the middle of October, after some days of cold, rainy weather, the first cases were noticed. In December, when Keen left the hospital, fifty cases in all had occurred, with but two deaths.

In 1863 an outbreak of hospital gangrene occurred in Annapolis, Maryland, among men who had recently been brought from Richmond, Virginia, all of whom had been closely confined in the prisons and prison hospitals of that city. "In the prisons they were much crowded, and the majority were unprovided with beds or cots, sleeping on straw which was foul and infected with vermin." In the epidemic at Nashville, Tennessee, in the same year, the disease appears to have been of an indigenous origin. The cellar under the hospital had passing under and opening into it by several apertures the common sewer of that part of the city. The soil-pipes of the several wards emptied into the sewer without traps. The cellar opened upon an alley from which the infected ward derived its ventilation. The emanations from the cellar were most offensive at all times. Surgeon Goldsmith in his report states: "I think that the records of surgery do not afford a more unique or striking example of one of the methods of the production of hospital gangrene."

A still more striking example of the conditions favoring the development of hospital gangrene is to be found in the experiences of the Union soldiers in the Confederate prison at Andersonville, Georgia. The site of this prison, which was simply a stockade, and which afforded no protection of any kind, was selected by General Winder and was enclosed in November, 1863. The ground covered was about fifteen acres, but the space taken up by the various walls and the dead-line reduced the space to about twelve acres. The ground, which sloped toward the centre on either side, was divided into equal halves by a small, muddy brook. A part of the valley thus formed was a swamp. The refuse from the cook-house and the sewage from the guards' camps were emptied into the brook, and thus rendered it unfit for drinking purposes, so that the prisoners relied chiefly upon wells which they made for the purpose. Every tree had been cut down and no shelter was afforded. No provision was made at first toward carrying off the refuse and sewage of the prison, and no sanitary regulations were put in force. "The only living things that seemed to thrive in this place were the flies, and they swarmed. Everything was covered with them, and they were responsible for the maggots that kept the swamp a moving mass of corruption" (Mann). According to Jones, a morass of human excrement lined the banks of the stream. The greatest number of men accumulated at any one time is said to have been thirty-five thousand, and, although the mortality was enormous, this number was maintained by the frequent arrivals of fresh squads of prisoners. In the summer of 1864, Lieut.-Col. D. T. Chandler of the Confederate service, who officially inspected the prison, begged the Richmond government to send no more prisoners. His report states:

There is no medical attendance provided within the stockade; small quantities of medicine are placed in the hands of certain prisoners of each squad or division, and the sick are directed to be brought out by sergeants of squads daily at "sick call" to the medical officers, who attend at the gate. The crowd at these times is so great that only the strongest can get access to the doctors, the weaker ones being unable to force their way through the press; and the hospital accommodations are so limited that, though the beds (so called) have all or nearly all two occupants each, large numbers who would otherwise be received are necessarily sent back to the stockade. Many—yesterday twenty—are carted out daily who have died from unknown causes and whom the medical officers have never seen. . . . . The sanitary condition of the prison is as wretched as can be, the principal cause of mortality being scurvy and chronic diarrhœa. Nothing seems to have been done, and but little if any effort made, to arrest it by procuring proper food— . . . . a place the horrors of which it is difficult to describe and which is a disgrace to civilization.

The report of Crews Pelot, Asst. Surg. C. S. A., states, in regard to the hospital accommodations:

"A majority of the bunks are still unsupplied with bedding, while a portion of the division tents are entirely destitute of either bunks, bedding, or straw, the patients being compelled to lie upon the bare ground." After describing the insufficient supply of food and medicine, he adds: "Our wards—some of them—were filled with gangrene."

During the month of August (1864), about the time when these reports were written, there were 31,678 prisoners in the stockade, and the number of deaths in that month amounted to 2993.

About this time Dr. Joseph Jones was sent to inspect the condition of the men at this prison. From his extensive and painstaking report are quoted the following details:

"In the depraved and depressed condition of the system of these prisoners, in the foul atmosphere of the stockade and hospital reeking with noxious exhalations, small injuries—as the injury inflicted by a splinter running into a hand or foot, the blistering of the arms or hands in the sun, or even the abrasion of the skin in scratching the bites of insects—are sometimes followed by extensive and alarming gangrenous ulceration."

Dr. A. Thornbury reports to Dr. Jones that in Ward No. 5 at the Andersonville Hospital 325 cases of gangrene were treated during the months of July, August, and September (1864), and that out of that number 208 died.

Gangrene first made its appearance in April of that year, and in many cases it was difficult to decide at first whether the ulcers were scorbutic or gangrenous. Small-pox also broke out at this time, and several thousand were vaccinated. As was to be expected, in every case affected with scurvy gangrene supervened in the vaccination-wound, and many of these cases died.

The origin of the gangrene appeared to depend in a great measure upon the state of the general system.

"In such a filthy and crowded hospital as that of the Confederate States Military Prison of Camp Sumter, Andersonville, it was impossible to isolate the wounded from the sources of actual contact of gangrenous matter. The flies swarming over the wounds and over filth of every description; the filthy, imperfectly washed, and scanty rags; the limited number of sponges and wash-bowls (the same wash-bowl and sponge serving for a score or more of patients),—were one and all sources of such constant circulation of the gangrenous matter that the disease might rapidly be propagated from a single gangrenous wound. . . . . In many cases gangrene attacked the intestinal canal of patients laboring under ulcerations of the bowels. . . . . Amputation did not arrest hospital gangrene: the disease almost invariably returned. Almost every amputation was followed finally by death, either from the effect of gangrene or from the prevailing diarrhœa and dysentery." The exhalations from the gangrenous wounds of the Federal prisoners in the hospital and stockade appeared to extend their effects to a considerable distance outside of these localities. Thus the Confederate soldiers guarding the prisoners, who did not enter the stockade or hospital, were in several instances attacked with hospital gangrene supervening upon slight abrasions or injuries. "In the gangrenous stumps examined after death the disorganization of the vessels and muscular tissue was widespread. Stumps from which gangrene had apparently disappeared, and which were thought to be doing well, were discovered after death to be thoroughly rotten within, notwithstanding that there was but little discoloration of the skin and comparatively little swelling. In the decayed state of the blood and in the depressed state of the forces gangrene appeared to affect the tissues with great rapidity and with but slight external marks of inflammatory action."

The extent of mortality of this epidemic of hospital gangrene will probably never be known accurately; but, as the testimony of Col. Chandler shows that many cases of severe illness never came under the eye of the surgeon at all, and as Dr. Jones concludes that scurvy directly or indirectly caused nine-tenths of the deaths among the prisoners, and inasmuch as it is known that for one month alone the death-roll amounted nearly to three thousand, and that it was often difficult to distinguish in the beginning between scorbutic and gangrenous ulcers, and that when the epidemic was at its height nearly every abrasion become gangrenous,—some faint idea may be gained of the enormous number of cases of gangrene that occurred. It is hardly necessary for the writer to say more about the rôle which bad food, unhealthy surroundings, and depressing influences play in the etiology of this disease.

The Franco-German War, with all its greatly perfected medical equipments in both armies, was not exempt from this plague. It will serve no useful purpose to go into any of the particulars of this campaign: a single example will suffice: In the hospital at Brest three separate epidemics of gangrene occurred, each one following the arrival of a convoy of wounded from the front.

It was not alone in time of war that this disease flourished, and, although Joseph Jones makes the statement that it was unknown in the South previous to the Civil War, the writer cannot help feeling that the disease nevertheless existed, but was unrecognized. The following statement, taken from Jones's report, at least suggests such a possibility. Writing from the general hospital at Staunton, Virginia (in 1863), Dr. Merillat says: "Fortunately, I have never had an opportunity of observing in this hospital the disease described in the books as hospital gangrene." He then proceeds to give an account of certain conditions of the wounds in his wards, which account is evidently a description of the ulcerating form of gangrene. Certain it is that the disease was familiar to hospital surgeons in Boston and in Philadelphia, as the writer can testify from personal knowledge. A most malignant epidemic at the Massachusetts General Hospital is one of the earliest recollections of his professional career. This epidemic occurred at a period when the river flats adjoining the hospital grounds were filled in. One of the peculiarities of this epidemic was the frequent complication of erysipelas.

The following case is taken from the records of October 1, 1864: Amputation of leg at junction of middle and upper thirds for osteosarcoma; on October 6, sloughing aspect of wound with exposure of both bones; on the 7th, chill; on the 14th, complete separation of flaps by sloughing. The muscles are separated for some distance from the integuments. Some hemorrhage from the main artery. Death occurred October 15. Many cases of amputation presented about this time very typical examples of the pulpy form. The wounds of stumps were enormously swollen and everted. Secondary hemorrhage was of frequent occurrence, and in several cases ligature of the femoral artery in Scarpa's triangle for hemorrhage was followed by gangrene of the ligature-wound, and death.

But few cases have been seen in the hospital since the introduction of the antiseptic methods. A case of the ulcerating type the writer saw, however, in the summer of 1889, in the wards, but failed to obtain from the surgeon in charge of the case a specimen for bacterial study. Unfortunately, at the time of the disappearance of hospital gangrene bacteriology had not reached that point of perfection which it since has, so that no satisfactory scientific work on the *relation of micro-organisms to the disease* has been accomplished.

The experimental work of Koch, although it is confined entirely to animals, is of sufficient value to be recorded here.

In Koch's experiments on septicæmia in mice he found in certain cases, in the neighborhood of the place of injection, in addition to the septicæmia bacillus, a micrococcus growth which produced a disease resembling gangrene. By using field-mice instead of house-mice he was enabled to eliminate the bacillus, as this organism would not grow in the blood of the former animal. The micrococcus growth, however, developed at the point of inoculation just as well in field-mice as in house-mice. He found the ear of the mouse the best place to study the influence of the coccus upon the tissues and its mode of growth. He says: "Spreading out from the place of inoculation one can see extremely delicate and regular micrococcus chains, here pressed together so as to form thick masses, there arranged diffusely, the individual elements of these chains, as can be understood from the measurements of the longer ones, having a diameter of 0.5μ." These organisms can be traced all through the gangrenous portions of the ear; here neither red blood-corpuscles nor nuclei of lymph- or of connective-tissue cells can be seen. Even the exceedingly resistant cartilage-cells are pale and unrecognizable. "All the constituents of the tissues look as if they had been treated with caustic potash: they are dead, they have become gangrenous. Under these circumstances the bacteria develop all the more vigorously, the micrococci penetrate in numbers into the damaged blood- and lymphatic vessels, and here and there the cocci fill the vessels so completely that they appear as if injected." Just beyond the point reached by the cocci is a densely agglomerated mass of nuclei, forming a wall, as it were, against the invasion of the micrococci. This wall has no great breadth, and immediately beyond it comes the normal tissue. The micrococci do not quite reach up to this layer of leucocytes. Between the two there is a layer of considerable breadth consisting only of gangrenous tissue, in which neither micrococci nor leucocytes are found; the cells of the layer of leucocytes adjoining this gangrenous tissue appear to be in a state of disintegration. Koch thinks that the organisms excrete a soluble substance which comes in contact with the surrounding tissues by diffusion. When greatly concentrated this product has such a deleterious action on the cells of the tissues that they perish. [A sort of coagulation-necrosis evidently takes place.] At a greater distance from the micrococci the poison becomes more diluted and acts less intensely, only producing inflammation. "Thus it happens that the micrococci are always found in the gangrenous tissue, and that in extending they are preceded by a wall of nuclei which constantly melts down on the side directed toward them, while on the opposite side it is as constantly renewed by lymph-corpuscles deposited afresh."

The close resemblance between the membrane of diphtheria and certain forms of hospital gangrene has raised the question of the identity of the two diseases. The diphtheritic inflammations, however, do not necessarily have any connection with the infectious disease known as "diphtheria." The diphtheritic membrane, such as is seen on mucous membranes or elsewhere, is due to a combination of necrosis and inflammation. It is an anatomical process which may be caused by the Klebs-Löffler bacillus, the organism that produces true diphtheria, or by the streptococcus, and possibly by other organisms. The action of the diphtheria bacillus is quite superficial, and it does not show a tendency to invade the deeper tissues. The presence of a diphtheritic membrane on an open wound does not therefore necessarily imply true diphtheria. The presence of streptococci in all other forms of membranous inflammations is a possible indication of what may be found in the diphtheritic form of hospital gangrene.

The latest microscopical studies of specimens of gangrene, taken from the recently-dead subject, are those of Heine, made probably about 1870—a period when little was known of the proper methods of bacteriological research. Sections examined with high powers of the microscope showed on the surface a finely granular homogeneous layer, varying greatly in thickness, which contained large numbers of chain-like organisms resembling "those described by some authors as micrococci." These organisms were seen sometimes in many-branched chains and sometimes in masses closely packed together. In the deeper portions of this layer were seen fragments of leucocytes (*Eiterzellen*), and deeper still were found masses of leucocytes closely packed together, the same organisms being found either in the cells or in chains intertwined between them. Wherever the leucocytes had broken down the micrococci were more visible. In this layer was also seen a fine network of fibres which at places were continuous with broad bands of coagulated fibrin running between the cells. Lower still he found a layer of granulation tissue rich in blood-vessels, in many of which coagulation of the blood had taken place. In places the walls of the vessels appeared to have broken down, and they were surrounded by circumscribed clots or by diffused infiltration of the surrounding parts with blood. The tissues near the wound appeared to be infiltrated for a considerable distance with leucocytes which were collected between the fat-cells, the muscular fibres, and the tendons, so that these structures were fairly buried in the infiltrating tissue, and their nuclei appeared to be undergoing a degeneration (coagulation-necrosis). The principal conditions observed by Heine were the larger numbers of micro-organisms, the marked tendency to coagulation of the intercellular substance and exudation fluids, the enormous accumulation of leucocytes, and the tendency to degeneration of the cells and coagulated intercellular substance in the final putrefactive changes.

The latest article on hospital gangrene is by Rosenbach. A careful study of two specimens sent to him from the Army Medical Museum at Washington showed that the preparations, preserved since the Civil War, were too old to make it possible to detect the presence of bacteria. Rosenbach reports in his earlier monograph two cases of traumatic gangrene in which the disease originated in a slight injury to the finger. Rapidly-spreading gangrene of the arm followed, and cultures taken from incisions made into the gangrenous portions showed the presence of the streptococci. In two cases of traumatic gangrene, with emphysema, of a most malignant type he was able to find, microscopically, a bacillus, but no streptococci. The cultures failed.

The writer mentions the following cases of traumatic gangrene—although clinically the disease is widely different from hospital gangrene—because they have a bearing upon a personal experience:

In 1883 the writer was summoned into the country to a case of traumatic gangrene following a gunshot injury of the leg. The disease had in forty-eight hours spread from the foot to the middle of the thigh, and the odor showed that putrefactive changes were well advanced. The operation of amputation in the upper third was performed at midnight. Proceeding on his journey the next morning, the writer met a physician in consultation in the afternoon, and explored a sinus communicating with a carious rib. A few days later a well-defined type of hospital gangrene was developed in the wound, which was not larger than would admit a good-sized drainage-tube, and before the disease could be checked an ulcer the size of a dessert-plate had formed. The only instrument employed in both operations was a pair of scissors, as, with this exception, the instruments of his colleague were used in the second operation. The scissors were employed to lay open the sinus where gangrene subsequently supervened. That they were the vehicle by which bacteria were transferred from one case to the other seems highly probable.

So far as the evidence goes, it would seem to favor strongly the assumption of a streptococcus bearing the same relations to gangrene that the streptococcus erysipelatis does to erysipelas. But the bacteriology of gangrene, after all has been said, from a modern point of view may still be regarded as almost a terra incognita.

As has already been explained, the disease is not confined to hospitals, but may occur in private practice. The records of nearly all hospital epidemics show that many of the cases were brought into the hospital with well-developed gangrene. At the present time it is much more likely to be met with outside the hospital, where antiseptic surgery has no control. Why cases are not brought into hospitals is a difficult question to answer. None are reported, although probably such occurrences do happen. It might be assumed that no epidemics exist at present, but with the present knowledge it is known that such surgical epidemics take their origin from favorable combinations of bad weather, filth, and crowded quarters. These combinations are not so difficult to obtain in every large city as to make the origin of sporadic cases of gangrene impossible.

The presence of extra-mural cases of gangrene in the city during a hospital epidemic may be accounted for by contagion, for the route which the virus takes is often a very circuitous one. An example of this is given by Brugmanns, who states that in 1799 a quantity of charpie was sent from France for use in the Dutch hospitals. Wherever these dressings were used gangrene occurred. Inquiry brought out the fact that the charpie had already been used for dressing wounds, and that it had been cleansed and bleached for the trade.

Much has been said about the contagiousness of gangrene. Medical literature contains too many examples of successful inoculation from man to animals and from man to man for the question to admit of any doubt.

Joseph Jones experimented upon a large pointer dog: about half an ounce of gangrenous matter was taken from the wound of a dead subject and was buried between the lips of an incision. The wound subsequently took on a typically gangrenous condition. Fischer made wounds in five rabbits and rubbed into the wounds the discharges from a gangrenous wound. In all cases gangrenous ulcers were produced. Dussaussoy treated an ulcerated carcinoma of the breast in a man fifty years of age with inoculation of gangrenous matter, the patient having refused to submit to the actual cautery. He dressed the sore for several days with charpie soaked in the gangrenous discharges, but without effect. He then decided to bruise the granulations and make them bleed, and then applied the matter to the freshly-made wounds, and in three days the ulcer had become gangrenous. This coincides with clinical observation that fresh wounds are more susceptible to the disease than those that are suppurating freely.

Ollivier in 1810 had his arm inoculated with gangrene during an epidemic in Spain. He visited for this purpose a locality where the disease existed. The matter was taken from the wound of a young soldier who finally died of the disease. It was inoculated with a lancet into the skin of the deltoid region, after which

Ollivier immediately returned home, distant a two-days' journey on horseback. Gangrene established itself in the puncture, and could only be controlled by the actual cautery.

The following is an example of contagion from patient to patient reported by Act. Asst. Surg. Cleveland:

In the officers' hospital an officer with gangrene occupied a room alone. The carpenters wished to put in a water-pipe, and he was removed to a room in which were three other officers with wounds not then gangrenous. All four had their wounds exposed and dressed, and the gangrenous odor pervaded the apartment. Although the officer was returned to his own room in an hour, the next day gangrene appeared in the wounds of the other three who had been exposed to the infection.

Many clinical observations are cited where cases in hospital wards have not communicated the disease to patients with wounds in the adjoining beds, while patients in distant parts of the ward were attacked. This inoculation can easily be explained by transportation of the virus by dressers and attendants. More difficult to explain, however, is the existence of two wounds in the same individual, one of the wounds being gangrenous, the other being healthy.

Asst. Surgeon Thomson reports the case of a soldier wounded by a fragment of shell which passed across the right thigh below Poupart's ligament, through the scrotum, destroying the right testicle, and behind the left thigh. The thigh-wounds were both superficial. The wound in the left thigh was attacked with gangrene. At this time there was in the right thigh a granulating surface, three by two inches in dimensions, level with the integument and cicatrizing rapidly. A smaller equally healthy surface remained unhealed upon the scrotum. The gangrenous ulcer continued to spread until it had involved the perineum and was eight inches in diameter, when it was finally controlled by treatment. In spite of the profuse discharge, the other wounds continued to cicatrize rapidly. Surgeon Thomson remarks: "If, therefore, the disease be propagated by inoculation, all the circumstances were favorable, since the proximity of the thighs at their upper part and a denuded surface on the scrotum, that might act as a link, render it certain that a portion of the great discharge from the left must frequently have been placed in contact with both of the other sores."

Such a case seems not difficult to explain on the theory of the protective influence of the granulations. A bruising of the sore on the posterior aspect of the body led to its inoculation from some outside source. The healthy state of the granulations of the other wounds served as a protection to them. Probably most examples of this sort, when analyzed, can be explained in some such way. They were usually made to serve as an illustration of the theory that hospital gangrene is a "constitutional disease;" that is, a disease not due to local contagion.

The question of the possibility of inoculation through the uninjured skin has been raised by Rosenbach, who points to Garré's experience with the inunction of cultures of the staphylococcus pyogenes aureus on the sound skin (p. 138). Very slight bruises are sufficient, as has already been seen. Gangrene is said to have occurred in the days of slavery after the use of the lash. Jones states: "Gangrenous spots followed by rapid destruction of tissue appeared in some cases in which there had been no previously existing wound or abrasion." It is not probable, however, that clinically gangrene is found developing in the uninjured skin.

That meteorological influences favor the outbreak of an epidemic of gangrene need hardly be said after the testimony of Macleod, of Keen, and of others already quoted.

The hot sirocco was always dreaded at Scutari, and the peculiar climate at Andersonville had undoubtedly much to do with the progress and virulence of the epidemic. The heat of a camp exposed to the full rays of a summer sun in Georgia, and the heavy rains of that region, combined to favor the growth of a bacterial poison. In the North the sudden advent of cold and stormy weather is frequently noted as immediately preceding an epidemic.

The *period of incubation* does not appear to be of certain duration. The observation of Cleveland quoted above would place it at as short a period as twenty-four hours. Rochard cites a case where one week is supposed to have elapsed between the performance of an operation with an infected instrument and the outbreak of the disease. In Ollivier's case of inoculation of his arm with the virus the characteristic appearances showed themselves first on the third day.

The *principal forms* which are described by modern authorities are the ulcerating and pulpy forms. The term "diphtheria of wounds" is also frequently used to denote a milder type which appears to affect the granulations only. Some regard this simply as a milder form of ulcerating or "phagædenic" gangrene; others are opposed altogether to the use of the term "diphtheria" in connection with gangrene, as the two diseases should not thus be confused with each other, they being two entirely distinct affections. Heine takes strong ground in favor of the identity of the two diseases. He bases his views partly on the frequent occurrence of diphtheria of the throat during epidemics of gangrene, and of cases of diphtheria following the reception of gangrene into hospital wards. During an epidemic at Heidelberg, Heine dressed the wounds for several weeks, during which time he had not seen a case of diphtheria. At the end of a month he was taken ill with diphtheria. During Heine's illness O. Weber, the noted surgical pathologist, took charge of his cases, and a few weeks later he also was attacked with diphtheria, which terminated fatally, although he had not previously been exposed to the disease. The present knowledge of diphtheria would enable one to determine in a similar case whether the disease was a form of infection with the Klebs-Löffler bacillus, or, what is more probable, was a mixed infection of other organisms.

A strong argument against the identity of the two affections is the alleged absence of paralytic symptoms following gangrene. Heine explains this by the relative nearness of the throat inflammation to the base of the skull, and by the ease with which such inflammation would extend to the nerves usually affected. Rosenbach thinks that this paralysis is not produced in this way—that from the present standpoint of our knowledge the paralytic phenomena must be regarded as the result of a ptomaïne-poisoning, and that the absence of such symptoms in gangrene implies the action of a different virus. Heine quotes, however, certain cases of gangrene where symptoms of paralysis have actually occurred, but his opponent regards these cases as not genuine gangrene, but as diphtheria of the wound. Felix inoculated wounds with the poison of diphtheria by dressing granulating wounds with charpie impregnated with fragments of membrane and secretions from cases of diphtheria. In two cases diphtheritic inflammation of the wound, of a moderate degree of severity, was produced. It is not denied that gangrene may not affect the mucous membranes, but it is claimed that in such cases the deep ulcerations and the characteristic conditions of the surrounding parts present a very different appearance from ordinary diphtheria.

Finally, the prevalence of diphtheria for nearly a score of years since the disappearance of gangrene is strongly suggestive of a radical difference in the exciting causes of the two diseases, and, inasmuch as it is known that a diphtheritic membrane can be formed by organisms which bear no relation to true diphtheria, there is now but little evidence to produce in favor of their identity.

In the mean time, guided by clinical appearances only, it will be best to distinguish a *diphtheritic form of gangrene.* This form may be regarded as the mildest type of the disease, and as one in which the granulations are chiefly affected, and in which there is an arrest of the healing process rather than destruction and enlargement of the area of the wound. The earliest change to be noted—and one which, in the writer's student days, the dresser was cautioned always to watch for carefully in every case—was a change of the granulations from their healthy red color to a grayish tint. There is at first a loss of color. The surface of the wound becomes glazed and somewhat opaque, forming a thin veil or membrane through which the contour of the granulations is still seen. The increasing opacity and thickness of this layer finally forms a sort of "rind," which occasionally develops without any accompanying symptoms of infective inflammation. This membranous condition of the wound may be caused by some accidental source of irritation, such as the retention of foul discharges, mechanical irritation, or the presence of a foreign body in a fistulous canal opening into the wound. What has occurred is chiefly a change in the character of the discharge from the wound with coagulation of the exudation on the surface. When, however, the disturbance in the healing process is more profound, as shown in alteration of the granulation tissue with distinct increase of irritation in all parts of the wound, in greater readiness on the part of the granulations to bleed, and in a more inflamed appearance of the margins of the wound, the surgeon may look for coagulation-necrosis involving the upper layer of the granulations, and consequently the development of a diphtheritic membrane. This membrane may involve a depth of tissue sufficient to produce necrosis of the surface to a considerable extent and the formation of sloughs, or there may be seen here and there small extravasations of blood due to the breaking down of the walls of the vessel which supplies the different granulations.

The secretion of the wound is at first diminished; later it changes in character and becomes more watery, and it is then much more abundant, so that in some cases the dressings become quickly saturated with the discharge and require to be changed frequently. The margins of the wound are not materially affected in the milder cases, but when the granulating surface becomes more deeply infected the edges of the ulcer are found thickened and raised, while at the same time portions of the membrane melt down or are thrown off as small sloughs. The wound assumes a crater-like appearance, and occasionally the edges of the skin begin to break down and have an appearance as if they had been gnawed by some rodent. Usually the process is arrested by treatment, and as the membrane melts away or is cast off the healthy granulations appear, and the swollen and somewhat injected lips of the wound resume their natural size and color, the cicatrizing process proceeding once more.

The type to be placed next in point of severity, but which writers generally regard as less frequent than either of the other varieties, is the *ulcerating form.* Here the formation of a membrane is not so apparent: the granulations, however, have an unhealthy appearance, are paler than usual, and have lost their plump, exuberant character. On closer inspection it is found that a number of them are the seat of minute dark-red or light-gray patches, which are sprinkled about over the surface of portions of the wound. These points soon break down and leave behind them clean-cut circular excavations in each granulation. Some of these patches look like small pustules, which, when they break, expose a grayish surface. These minute ulcerations subsequently run together and form an ulcer in the granulating surface. Several such ulcerations may develop in different portions of the wound, and when the process has extended to the outer border, the skin becomes involved and breaks down, leaving semi-circular defects which give the lips of the wound the appearance of having been bitten out. At this time the surface of the wound becomes discolored and assumes a grayish or a brownish hue, the discharge becoming thin and streaked with blood and having a foul odor. The process is not usually a rapid one, and the breaking down and enlargement of the wound may be an affair of several weeks. In this way the wound may increase in size indefinitely both in area and in depth. The extent to which the ulcerating process will penetrate depends somewhat upon the anatomical nature of the tissues. A dense fascia will exert a limiting influence, but when loose connective tissue is involved muscles may be dissected out or be eaten through. In the case reported by Thomson, already quoted, the condition of a wound of the posterior portion of the thigh is thus described:

"An ulcer three by two inches in extent was found, oval in shape, covered with an ashy-gray slough upon its margin, thickened and everted, surrounded by a livid areola, and, instead of normal pus, discharging a thin fetid serum mixed with débris." This description portrays fairly well the diphtheritic type. Attempts to treat it with applications of nitric acid were unsuccessful, and the report continues:

"There was the characteristic margin preceded by the areola of livid stasis preparing the tissues for their rapid destruction. The connective tissue beneath the skin had been destroyed, so that the skin for an inch from its margin was perfectly movable. The muscles, separated from each other by the death of their connective tissue, lay in the wound, bathed in its discharge, but rosy and florid and resisting the advance of the disease. This sore was so unmistakably hospital gangrene that several pictures of it were taken by direction of Surgeon Bristow, which represent well the surface of the ulcer dripping with its thin, serous discharge, mingled with threads of dead connective tissue, its 'piled-up,' thickened, and everted margin surmounted by a thin line of vivid redness, and its broad zone of purple congestion shading away into a bronze hue, the depth of color in the areola indicating the engorgement of the small vessels, and its hue the feebleness and slowness of the movement of the blood. . . . . But little change had taken place in the character of the ulcer, which was eight inches in length by seven in breadth, extending to the perineum and irregularly oval in shape. The muscles exposed (the semimembranosus and biceps) had yielded, and were now almost divided." The interval of time which had elapsed during which the changes described had taken place was a little over two months; from this time on convalescence took place.

A case like this may be regarded as a somewhat severe example of the ulcerating form, but the appearances of the skin around the wound are such as are to be expected when the ulcerating type has reached its full degree of development. Frequently, however, the disease is confined to a superficial form of ulceration, and then there would be seen but little sloughing or membrane-formation. The wound has a dirty, unhealthy, or sometimes only an irritated look, and is constantly growing larger until arrested by treatment. The different phases of phagædena are well portrayed by this type of gangrene.

The striking results of phagædenic ulceration are well shown by Plate xxvii. of the *Surgical History of the War of the Rebellion*, where a portion of the calf of the leg has been eaten to the bone, laying bare the popliteal artery at its lowest portion. The wound looks as if it had been produced by the teeth of some wild animal.

These examples are, however, suggestive of those forms which may be said to come between the ulcerating form and the characteristic and commonest type of hospital gangrene—"*the pulpy form.*" This variety includes all the graver cases with extensive and deep-seated loss of tissue.

The pulpy form may begin with a diphtheritic infiltration of the granulations, which infiltration rapidly swells to a thick and œdematous covering of the wound, or the color of the granulations deepens, owing to an intense hyperæmia of the part. Under the increased blood-pressure many of the tender walls of the blood-vessels give way and diffuse extravasations take place, or, as Pirogoff describes, hæmatomata may form rapidly, owing to profuse bleeding in the granulation tissue at certain spots. This form is sometimes called the "hemorrhagic." Whatever the preliminary changes may be, the surface of the wound soon becomes enormously swollen, and it is changed into a dirty gray or a greenish mass of putrefying sponge-like tissue. The secretion of the wound, which was at first arrested, now begins to run again. It wells up through the pulpy mass in the form of fetid ichor, the odor of which is thought by many to be quite characteristic. The edges of the wound become extremely sensitive, and they are everted and raised and of a deep-red or purple tint, shading off, when the disease is spreading, into a bronzed hue. Changes as profound as these may occur within from twenty-four to forty-eight hours. The swollen membrane thus formed soon begins to putrefy, but it does not readily separate. Its color changes frequently, and it is difficult to describe. It is often distended with gas from the decomposing substance, and it finally breaks up into soft, gelatinous sloughs or moist, cheesy débris, and is thrown off, only to be followed by new formations beneath it. In the mean time the deeper tissues have been attacked, and the advance of the infection is indicated by the increased amount of inflammatory reaction, as shown by the great swelling, the discoloration of the surrounding integuments, and the profound constitutional disturbance. At this time secondary hemorrhage from some large vessel frequently takes place, speedily terminating the case fatally or necessitating the ligature of the femoral or brachial or other vessel of largest size, thus involving the formation of a wound in which gangrene may develop itself anew. The changes described are taken from personal memory of cases which occurred in the epidemic of the hospital to which reference has already been made.

The differences that may occur in the form of the exudation are of course very great, each epidemic showing peculiarities of its own. Rosenbach describes a gelatinous membrane which occasionally forms enormous colloid vegetations. When in a state of putrefaction such voluminous masses have been likened to decomposing fœtal brains.

The discharge from the wound is enormous; it may be orange-colored or may be brownish, or—what is a more generally fitting description—it may be foul and dirty. Pitha says of it: "No matter how deep the infiltrated surface appears to be, it always seems insufficient to account for the great quantity of the discharges. . . . . The foul pus pours in such cases as if it came from an inexhaustible spring."

As the infection advances no tissues are spared: the muscles are laid bare, and they often so swell and soften, as they are rapidly eaten through, as to suggest the presence of a sloughing sarcoma. The nerves are dissected out, but they generally retain their anatomical form and distribution. The fasciæ are more resistant, but they do not long resist the advance of these graver types of the disease. Articulations may be laid open, and even the bones may not escape necrosis. In some of the most malignant types the greater portion of a limb may thus become disorganized, but these cases, fortunately, are rare. The skin has a marble hue, the parts are distended by emphysema of the connective tissue, and mortification of the limb may ensue.

The great swelling which takes place in the different layers of the wound is often deceptive as to the amount of tissue which has been lost. This is shown after the membrane separates and the wound rapidly contracts.

The disease does not always advance with the rapidity indicated. Even cases which eventually may terminate fatally may begin and advance with great deliberation until, as the vital powers become lowered, the gangrene seems to gain new strength and to assume a more malignant type.

The early writers generally state that at first constitutional symptoms are wanting, but this is probably due to the fact that thermometric observations were not taken. It is not, however, until the second week that the symptoms become marked. The fever-curve is of course variable, corresponding more or less with the local manifestations. It is quite irregular—more, as Heine says, like an outline of the Alps. The constitutional symptoms are probably produced by the absorption of the toxic products, or possibly by the bacteria themselves, and the fever does not differ clinically from that of septicæmia. But, although the typhoid-like condition with diarrhœa is characteristic of both affections, in gangrene there is a marked clinical feature in the great sensitiveness of the wound. The pain and nervousness attending the dressing of the wound are such, in some cases, that few men possess the fortitude to go through the ordeal. The bare idea of a change of the dressing may bring on, according to Pitha (whose patients were probably Southern Germans), convulsive trembling, perspiration, and palpitation of the heart. It is often necessary to etherize the patient at these times, especially when escharotics are applied. It is not surprising that many cases are followed by relapse, or that patients who have been discharged from the hospital as apparently cured have returned with the disease in full bloom again. Such a reinfection could easily take place from germs concealed in some part of the patient's person.

Among the most frequent complications of the disease is erysipelas; and if it may be supposed that they are both caused by the streptococcus group of organisms, it is certainly not surprising. With such a severe infective form of inflammation as gangrene, it is also to be expected that pyæmia may occasionally be met with, but this complication would probably not supervene unless local phlegmonous inflammations had followed or complicated the original disease.

A few selected cases may perhaps give a clearer idea of the cause and peculiarities of the pulpy form of gangrene:

Thomson reports a case of amputation of the thigh for a fracture of the tibia caused by a Minié-ball at the battle of Fredericksburg. The wound had healed, except a narrow strip of skin, on February 18, when it was found covered with a gray slough and had the characteristic odor. The cicatricial tissue soon yielded to the sloughing, and the subcutaneous connective tissue had been destroyed for two inches beneath the skin at the outer angles of the original incisions. The destruction was limited to the connective tissue until the nineteenth day, when the skin became involved. The constitutional symptoms became grave; the mental despondency was marked; a free diarrhœa also began. The whole surface of the stump had now a margin of black mortification of the skin, outside which was the usual areola of purple congestion, the complete stasis of to-day becoming the sphacelus of to-morrow. The end of the femur, protected by rosy granulations, now protruded from the black mass of sphacelus, the integument having become loosened by the destruction of the subcutaneous connective tissue, and retracted. The presence of this mass of putrefaction seemed to add to the nervous prostration, if, indeed, the absorption of such peccant material is not its sole cause. On the thirty-first day the symptoms had been typhoidal for several days: emaciation had gone on rapidly; there had been subsultus tendinum and muttering delirium with extreme prostration until this date, when death occurred. The limb was removed after death, and the specimen sent to the Army Medical Mnseum (Specimen 1000, Surg. Sect.). The sphacelus had involved all the tissue for five inches above the divided bone, and there seems to have been a faint effort to form a line of demarcation.

An interesting point illustrated by this case is the presence of healthy granulations at the end of the bone in the centre of the gangrenous mass. This is a peculiarity noticed by many writers—namely, that a portion of a wound may be affected with the disease, and in another part the granulations may be in a perfectly healthy condition. Jones reports a large number of cases in great detail. The following case is illustrated by two colored plates:

A man twenty-two years of age, who had been in the Confederate service nearly four years, was wounded in the middle of the left thigh (Aug. 17,

1864) by a piece of lead, weighing about a pound, from a rifle-shell. He was removed from Atlanta to Macon, and the disease appeared four days after his arrival at the latter place. On the fourteenth day the wound in the thigh was eight inches in diameter, was nearly circular, and was deeply and irregularly excavated; the edges were everted and the surface was coated with a dirty grayish, purplish, and dark-bluish leaden-colored layer. There was a most fetid, irritating, and sanious discharge from the wound, but no pus. Temperature 105.6° F. The next day the large muscles of the thigh were exposed by the gangrenous excavation, and they were frequently observed quivering, especially after the application of nitric acid, which causes intense pain. On the twenty-fifth day the wound began to assume a healthy appearance, and on the thirty-fifth day it was cicatrizing.

The next case, which is an example of the ability of gangrene to lay open joints, is quoted from the same author:

The patient was thirty-seven years of age. A Minié-ball struck the fleshy part of the forearm about the middle: no bones were injured. This injury occurred July 20, 1864, the patient being transferred from Atlanta to Macon. At the end of a month, when the wound was healing, it took on gangrenous inflammation, became swollen, and was surrounded by a red, livid areola and burned most painfully. By the middle of September the muscles of the arm and forearm in the region of the elbow-joint were extremely denuded and the gangrene was spreading. Application of nitric acid did not arrest it. October 1, the gangrene had denuded the condyles of the humerus and had penetrated the joint. The muscles exposed presented red, purplish, and greenish colors in different portions. The odor of the wound was insupportable. There were great prostration, dejection, and nervousness with muttering delirium. Tongue was dry and of a dark purple-and-blue color. October 4, hemorrhage from the brachial artery, near where it divides, took place at sunrise, and the patient died in twenty minutes.

Dr. Jones dwells upon the sallow hue of the complexion and the livid-blue color of the tongue as derangements manifestly induced by the gangrenous poison on the constitution of the blood. Perhaps the most striking examples of the severest type of the disease are related by Macleod:

"In the Crimea, during the summer of 1855, after the taking of the quarries and the assault in June on the Great Redan, not a few cases of amputation of the thigh were lost from moist gangrene of a most rapid and fatal form. In the case of a few, who lived long enough for the full development of the disease, gangrene in its most marked features became established, but most of the men expired previous to any sphacelus of the part, overwhelmed by the violent poison which seemed to pervade and destroy the whole economy."

Two cases under Macleod's own care, in men who had a limb utterly destroyed by round-shot or by grape, are thus described: "During the night previous to death the patient was restless, but did not complain of any particular uneasiness. At the morning visit the expression appeared unaccountably anxious and the pulse was slightly raised. The skin was moist and the tongue clean. By this time the stump felt, as the patient expressed it, heavy like lead, and the burning, stinging pain had begun to shoot through it. On removing the dressings the stump was found slightly swollen, and the discharge had become thin, gleety, colored with blood, and having masses of matter like gruel occasionally mixed with it. A few hours afterward the limb became greatly swollen, the skin tense and white, and marked along its surface by prominent blue veins. The cut edges of the stump looked like pork. Acute pain was felt. The constitution had by this time begun to sympathize. A cold sweat covered the body, the stomach was irritable, and the pulse was weak and frequent. The respiration became short and hurried, giving evidence of the great oppression of which the patient so much complained. The heart's action gradually and surely got weaker till, from fourteen to sixteen hours from the first bad symptom, death relieved his sufferings."

In regard to the *pathological anatomy* of the disease little remains to be said. The post-mortem appearances are those which are the result of septicæmia, unless pyæmia has occurred as a complication. In this case it is probable that in the neighborhood of the wound there would be evidence of phlegmonous inflammation.

One would hardly suppose that there would be any difficulty in the *diagnosis* of the disease, yet in its early stages there are conditions of hospital wounds which might be mistaken for gangrene. The mechanical or the chemical irritation of the granulations may be the result of unsuitable dressings, such as were frequently applied in former times. There may be obtained in this way capillary hemorrhage with œdema of the granulations, and even the formation of a croup-like layer. The writer has at the time of this writing a wound of the bursa of the elbow that has assumed such an appearance from hardening of the secretions in the dressing, which had been kept on a week. The presence of a foreign body or of a piece of dead bone, especially if the sequestrum consist of a fragment of cancellated bone with decomposing matter retained in its meshes, may also cause doubtful appearances of the wound, and even the formation of a rind upon the surface of the granulations. Such a rind is not infrequently seen in feeble or in aged individuals, or it may be due to the presence of a scorbutic or tuberculous taint in the tissues or in the system. Occasionally bedsores will counterfeit closely the appearances of hospital gangrene in the spreading of the wounded surface and in its sloughing condition. The writer has seen carbuncular sloughs transform a wound into one of this appearance, and show a tendency to spread which could only be checked by thoroughly cleansing and disinfecting the wound. This condition occurred in a feeble old man.

The "gray look" of a wound which has hitherto been healing kindly must be regarded as suspicious, particularly in times of epidemics, and formerly it was a condition that was always regarded with great distrust.

The *prognosis* of the disease is very variable. It must not be supposed from the clinical description given above that the mortality is greater than septicæmia, pyæmia, or tetanus, for instance. It is undoubtedly as serious a wound-disease as erysipelas, and perhaps more so, although such epidemics of erysipelas as occurred in America about fifty years ago have been of the gravest character. The ulcerating form is much less dangerous than the pulpy form, and the latter type varies greatly, according to its locality, in its effect upon the system. Penetration of the great cavities, such as the peritoneum or the pleura, by gangrenous ulceration is almost invariably followed, according to Packard, by a fatal termination. The opening of a joint during the progress of the disease cannot be regarded in any other light than as a most serious complication. In the epidemics observed since the beginning of the present century the mortality has varied from 18 to 80 per cent. In some of the more recent campaigns the mortality has probably been at a much lower figure.

The number of cases of gangrene reported in the *Surgical History of the War of the Rebellion* was 2642. Of these cases, 1142 were fatal, making a mortality of 45.6 per cent. The percentage of fatality (with the exception of penetrating wounds of the trunk) of cases of gangrene after flesh-wounds was larger than that after fractures. In one of the more recent epidemics, which occurred in the barracks at Berlin, the mortality was only 6 per cent.

In undertaking the *treatment* of hospital gangrene it is important to remember that the agent employed must come directly in contact with the diseased tissue—that it will be of no avail to dress the wound simply with applications containing an efficacious drug. The dead portions on the surface must first be removed, the membrane be scraped away, and sinuses be laid open, in order that the remedy may be enabled to exert its influence directly upon the diseased part. It is pre-eminently a disease where heroic treatment is clearly indicated.

The actual cautery has always been popular with the French surgeons. Pouteau was the first to endorse it. He says: "Cette pratique était familière aux anciens: osons la rétablir dans tout son lustre." Rochard says: "The actual cautery is more terrifying than painful. At a white heat and passed rapidly over the tissues it is less painful than applications of perchloride of iron. The cautery may be followed by the use of cold compresses removed from time to time until the pain ceases." At the present time the most suitable dressing to follow this would be an antiseptic poultice frequently renewed and alternating with an antiseptic bath until the separation of the sloughs has taken place.

Nitric acid in full strength, which has been much used, seems to have been the favorite application by Southern surgeons during the war. Jones advises a liberal and thorough application of the acid: "It should not merely coagulate and alter completely the gangrenous matters, but also come in contact with the sound parts. . . . . In most cases one thorough application of the acid will be sufficient. . . . . If, however, the patients be retained in the crowded wards or tents, the most energetic treatment will fail entirely of arresting the disease."

The patient, as in the case of cautery, should be placed under the influence of an anæsthetic and all gangrenous tissues should carefully be cut away. All sinuses found under the skin or in the connective tissue should be laid open freely and the dead tissues be removed. As Keen says: "Stumps must be laid bare and apparently ruined; sinuses must be fully exposed and the disease relentlessly pursued to its farthest refuge." Rochard well adds: "Il faut du courage."

For milder cases an acid wash may be used consisting of solutions of hydrochloric acid of greater or lesser strength; the one in use for many years at the Massachusetts General Hospital during epidemics was the following:

℞. Potass. chlor.,	℥ss;
Acid hydrochlor.,	ʒj;
Misce et adde.	
Aquæ,	℥viij.—M.

It can be applied on charpie.

Keen used chiefly in the West Philadelphia epidemic the acid nitrate of mercury, preferring it to nitric acid, as it caused less pain and often saved time by enabling the surgeon to dispense with an anæsthetic: "The pain continues for a shorter time, the slough appears to be destroyed and disintegrated more thoroughly, and it separates in from twelve to thirty-six hours sooner than that from the acid." He continues: "The constitutional treatment is, I take it, of far less importance than the local, just as the constitutional symptoms are less grave than the local. Frequently they will subside entirely after the vigorous local treatment advocated. The fever will abate, the patient will sleep well, the tongue clean, the bowels relax, and he will tell you the next morning that he has eaten an excellent breakfast and 'feels first-rate.'"

The application of pure or fuming bromine was advocated strongly by Goldsmith. This drug should be applied with great thoroughness. It at once obliterates all gangrenous odor; its ready vaporization permits its application to the bottom of the sinuses and sulci which cannot safely be laid open with the knife. Its action is almost instantaneous. Surgeon Cleveland was in the habit of applying bromine to all cuts or injuries of his fingers, and he had no trouble with such wounds, although coming into daily contact with the disease. Goldsmith advises for milder cases the following solution of bromine:

℞.	Brominii,	℥j;
	Potass. bromid.,	gr. 160;
	Aquæ,	ad ℥iv.—M.

Lint saturated with this solution should be applied to the part; over this a dry piece of lint; over this a sheet of lint spread with simple cerate; and outside of all a piece of oil-silk, which is intended to retain the vapor as long as possible. If the sloughs are thick and they cannot well be trimmed, the bromine may be introduced into the thickness of the slough by means of a hypodermic syringe. The irritating effects of the vapor of bromine upon the eyes and the air-passages of the dresser were such as to give a great deal of unpopularity to this remedy. It was employed, however, with great success in many of the army hospitals during the war, and afterward in civil practice, and those who had occasion to give it a fair trial were enthusiastic over its thorough work.

The French used perchloride of iron in their last war with success; it was the most successful remedy at Brest. Charpie soaked with it should be applied to the cleansed wound, and be renewed at the end of every twenty-four hours for a longer or shorter period. Its application appears to have been quite as painful as that of the much more powerful remedies.

Packard recommends the use of sugar—a carbohydrate not giving up its oxygen—which prevents oxidation and which acts as a preservative. Powdered white sugar may thoroughly and thickly be dusted over the wound or be applied as a thick syrup. "The cure consists in the removal of all sloughing and dead tissues, and in opposing oxidation by means of a dressing with any substance which either contains no oxygen or will not give it up."

At the present time the vast array of modern antiseptic remedies, among which we may mention iodoform and peroxide of hydrogen, will be at hand for the surgeon's use. Of these remedies, carbolic acid has already been employed in several epidemics. In weak solution it does not penetrate sufficiently deep. Heuter used 5 to 10 per cent. solutions, and reapplied them several times a day. In this shape it has a caustic action, but it was apparently not adapted to severe cases. It goes without saying that the most powerful prophylactic treatment is the application of the laws of strict asepsis so far as they can be carried out. If a single case occurs in a hospital ward, it should immediately be isolated; if a number of cases occur at once, the ward should be evacuated. An epidemic at the Chestnut Hill Hospital, near Philadelphia, was arrested in twelve hours by placing all those attacked with the disease in tents in an adjoining grove. A chronic case which has obstinately resisted local treatment will often improve rapidly after a complete change of room, of bedding, and of clothing.

Amputation for hospital gangrene of stumps was a frequent resort in pre-antiseptic days. There is no doubt that the presence of gangrene is no contraindication to such an operation at the present time. With thorough antiseptic precautions the case ought to do well afterward. In 1870 such an attempt was made by a German surgeon for gangrene of the foot involving the tarsal joints. The wound was soaked with a strong solution of carbolic acid, and the foot was carefully wrapped up in cloths wet with the same solution. The leg was thoroughly washed with "phényle-water" before the operation. The dressing for the stump consisted of carbolic compresses. The healing was slow at first, but after the opening of a small pus-cavity cicatrization rapidly took place.

XVIII. TETANUS.

Tetanus (from τιτάινω, to bend) is an infectious disease, generally traumatic in origin, characterized by painful tonic contraction of the muscles, beginning with those of the jaw or the neck and affecting progressively the muscles of the trunk and the limbs. It is accompanied by convulsive paroxysms and an irritation or inflammation of the nerve-centres in the upper portions of the cord. It is due to the presence of a bacterial poison in the blood and tissues.

The etiology of the disease has received a vast amount of study by modern as well as by ancient writers, and its origin has been attributed to various causes. One of the causes to which the disease has most frequently been attributed are sudden changes in the weather, particularly change from heat to moist cold. After the battle of Prague there was said to be as many as a thousand cases of tetanus among the wounded who were left upon the field of battle without shelter. In the Austrian campaign of 1866, Stromeyer saw thirteen cases after a cold storm which followed a period of heat. At Strasburg, Poncet did not see a single case of tetanus during the early period of the siege, but in September, after a sudden fall of the thermometer, a dozen cases occurred in the military hospital in which he was stationed. In tropical countries the disease appears to be much commoner and to favor certain regions. Negroes are supposed to be peculiarly susceptible, among whom, in Brazil and Peru, the disease is said to be very common. In Algeria the Arabians are supposed to enjoy an immunity to the disease; such at least is the experience of French surgeons. Idiopathic tetanus is said to be common in the Southern United States, in Central America, and in the West Indies: in Europe tetanus has most frequently been observed in connection with military surgery.

It has also been supposed that the disease might originate from an injury to some nerve-trunk. One of the most acute and typical forms of tetanus under the writer's care followed a lacerated wound of the arm with exposure of the median nerve for several inches in its length, in a way that rendered it impossible to cover the nerve with the integuments; but Weir Mitchell reports that tetanus from injury to the nerve-trunk occurred in only one case out of all that he observed during the late war, and he believes that the source of irritation is in the peripheral branches of the nerves in the majority of cases. Such a reflex origin of the disease has been assumed by several authorities, and the sometimes almost instantaneous relief of symptoms by the division of painful cicatrices or other sources of nerve-irritation gives ground for this belief. In the report of a case in the Surgical History of the War the symptoms were apparently due to such a cause, following amputation of the finger. Several months after there appeared tetanic symptoms, which were immediately relieved by the removal from the cicatrix of a neuroma about the size of a buckshot. The history of this case renders the diagnosis doubtful, but the association of the symptoms with the peripheral irritation is at least suggestive.

In another case, where the median nerve was caught in the cicatrix, intense pain was suffered and there was great nervous irritation after the wound had healed. Partial trismus occurred finally, that was somewhat relieved by an incision which freed the nerve from the cicatrix. The tetanic symptoms recurring were not relieved by resection of the nerve, and amputation was resorted to, after which the man recovered. Larrey divided certain cicatrices of the shoulder that gave rise to cramp-like pains and tetanus, the operation being followed by immediate relief of all the symptoms. "The patient opened his mouth and was cured." Rose refers to such cases, which he calls "scar-tetanus."

Following out this idea, some writers thought that the situation of the wound played an important part in the origin of the disease, and an endeavor was made to establish the fact that it was as a complication of wounds of the hands and the feet that tetanus was almost invariably found; but examination of statistics shows that this view is not borne out by the facts of the case, that the disease may follow injury in almost any region of the body, and that it may arise spontaneously when no perceptible wound is to be found. The view that tetanus was of humoral origin has been advocated by Travers, Billroth, and others for a long time. This theory assumed an intoxication due to the formation of a poison developed either in the wound or in the perspiration—in other words, a ptomaïne. An attempt was not made, however, to associate this chemical product with the development of bacteria.

It was not until 1885 that the bacillus tetani was discovered. It is a long, slender rod, in one end of which a spore forms, distending the cell into a "drumstick" shape (p. 54). It is one of the most marked types of anaërobic bacteria, and it is usually found mingled with several other varieties, from which it has been separated with great difficulty. For this reason pure cultures have only quite recently been obtained. The organism is found principally in the tissues near the wound, and it has not been satisfactorily demonstrated in either the blood, the internal organs, or the central nervous system. Injected into animals after cultivation, the organism produces symptoms of tetanus in twenty-four hours. At the autopsy a slight infiltration is seen at the point of injection, but no coarse changes are seen elsewhere. A few bacilli are found near the point of injection, but none in other parts of the body. In no case do their numbers stand in any proportion to the severity of the symptoms. For this reason it has been assumed that the organisms manufacture at the point of inoculation an extremely active poison which disseminates itself throughout the body. Betoli mentions the fact that slaves died of tetanus after having eaten the flesh of a bull which had perished from that affection.

Brieger has, in fact, succeeded in obtaining from the culture of the bacteria ptomaïne which he called "tetanine." The same substance he also obtained from the freshly-amputated arm of a man afflicted with the disease.

Under what special conditions infection takes place in man cannot yet be stated with any certainty. The tetanus bacilli are found in large numbers in the world about us—in garden soil, in the dust and sweepings of our streets and dwellings, in crumbling masonry, in putrefying fluids, and in manure. In connection with the latter source it may be mentioned that French writers, and particularly Verneuil, regarded persons who are brought in contact with horses as particularly susceptible. Considering the great numbers of tetanus bacilli that are constantly to be found about us, it might seem surprising that tetanus is so rare a disease. This is explained by their anaërobic nature. The presence of free oxygen prevents the development of the bacteria. The bacilli are therefore unable to find an opportunity to grow upon small and superficial wounds except in rare instances. Punctured wounds lodge the organisms deep in the tissue, a soil better fitted for their growth. If the penetrating foreign body, such as a splinter or a nail, should carry in with it dirt from the skin, grains of sand, or fragments of stone, the conditions are peculiarly favorable for the inoculation and development of the bacilli. Among the predisposing causes of tetanus may be mentioned age. Yandell shows that the disease is peculiarly fatal to persons under ten years of age, and that this period included 7 per cent. of all the cases collected by him, but did not include trismus nascentium. The disease is said to be rare in later life, but the same author noted fifteen cases occurring in individuals over fifty years of age; and one case is reported in a man aged eighty-nine. The condition of the patient's health is an important factor in his ability to resist the inroads of the micro-organisms. The enormous number of cases reported after the battle of Prague, although doubtless greatly exaggerated, indicates that exhaustion and exposure produce an enfeebled vitality peculiarly favorable for the origin of tetanus. Doubtless meteorological conditions favor the growth of the bacillus of tetanus, and under certain combinations it can easily be imagined that the disease might assume an epidemic form. Epidemics of the disease have not only been reported in literature, but it is probable also that every hospital has had several cases occurring within comparatively short periods of one another. Such has certainly been the writer's experience.

Tetanus may be traumatic or be idiopathic, according to the current authorities of the present day. In view, however, of the latest investigations, there may be reasonable doubt of the existence of the latter variety. As in erysipelas, it is not difficult to assume the presence of some small wound in which the organisms may have effected a lodgment. Cases of tetanus arising from so trifling an injury as a hang-nail have been reported, and the disease may become a complication of an internal injury, as a simple fracture. It is not improbable, therefore, that in the form of dust the organisms may be inhaled or be swallowed, and that subsequently an intravascular infection of the injured tissues may occur. A more important distinction is that made between *acute* and *chronic* tetanus. Puerperal tetanus and trismus nascentium are varieties usually considered as a group by themselves, but they are in reality not distinguished etiologically from traumatic tetanus.

Acute tetanus usually appears during the first week of the period of the healing of a wound. Yandell found that of 415 cases the disease supervened in two weeks in 196 cases. In the remainder—that is, those in which the disease appeared after the fourteenth day—the recoveries exceeded the deaths. As chronic tetanus is much more liable to terminate in recovery than the acute form, it is probable that in most of those cases in which the symptom appeared late the disease ran a chronic course. Of 367 cases reported in the Surgical History of the War, 287 occurred during the first two weeks after the injury or the amputation.

Sometimes, then, during the first or the second week of the convalescence from an injury, without any warning as shown by the state of the wound or the general condition of the patient, the first stage of the disease makes its appearance. After a comfortable night's rest, probably the last the patient will have, he awakes with a sensation of having taken cold. He complains of a stiff neck, but thinks little of it. Such a complaint on the part of the patient should put the surgeon on his guard, for, although it may be a symptom of a slight ailment only, it is almost the invariable precursor of the other symptoms of tetanus. During the day there is in the muscles of the jaw a slight stiffness, which renders it difficult for the patient to open his mouth. This stiffness is not painful, and it may still be regarded by the patient as a trivial matter; but this stage of comparative comfort does not last long, as the disease progresses apace. There is soon pain in the muscular contractions, which now become so powerful and continuous that the jaw cannot be opened and considerable difficulty is experienced in swallowing even liquids. In the mean time the "stiff neck" has included all the muscles that hold the head and the neck to the body. On examination of the jaws the masseters are distinctly felt in a state of rigid contraction, as hard as iron and with well-marked borders. Attempts to approach the chin to the sternum directs attention to the rigidity of the muscles at the back of the neck. If the hand is now passed down to the abdomen, the parietes are felt as firm and rigid as a metal plate; before the day closes the muscles of the back may already be affected, and the patient is unable to lie upon his back owing to the arching of the spine, or the opisthotonos, thus produced. There is already retention of urine, which, when drawn with the catheter, appears to be abundant and of a normal color. The distress of the patient has now become great, owing to the painful nature of the muscular spasm, which is not only extensive, but is also continuous; that is, "tonic." Attempts to swallow cause pain and distress, owing to paroxysmal increase in the muscular contraction. After a sleepless night the patient the next morning is found well advanced into the stage of full development of the disease. The locking of the jaws is as complete as before, and nearly all the voluntary muscles of the body except those of the upper extremities are involved. The arms may also be involved, but only to a partial extent. The lower extremities are rigidly extended. The patient is now extremely sensitive to disturbance of any kind: attempts to move him in bed, to administer nourishment, or to pass the catheter bring on a paroxysm of convulsive action of a most painful character. Even the muscles of the face are affected; the eyelids are seamed, the nostrils are raised, and the mouth is puckered in a peculiar way, while its corners are drawn back by the contraction of the cheeks. The eyes are drawn in and partly closed, and occasionally there is strabismus. The expression, which is peculiar to itself, can be likened neither to that of pain nor that of mirth. The so-called "sardonic grin" (*risus sardonicus*) is perhaps the best term that can be applied to it. Once seen by the surgeon, it is never to be forgotten. The writer remembers having seen the typical *risus* in one only of the cases that have been under his care. Poncet remarks that the surgeon in charge would never be able to recognize his patient after recovery. Poland mentions a case where the disfigurement remained after convalescence, and was still quite marked after a period of eleven years.

While all the muscles mentioned are still in a state of tonic spasm, there will be waves of convulsive spasm throughout the body, produced by any disturbing influence: these spasms now become more frequent and violent. The muscular contraction at this time is extremely painful, and any attempt to prevent it or to straighten the limb may lead to rupture of the muscular fibre. Larrey reports rupture of the rectus abdominis muscles owing to violent spasms brought on by putting the patient into a cold bath. The same accident is mentioned by Curling, and Dupuytren has observed rupture of the muscles at the back of the neck. Desportes records double fracture of the neck of the femur from muscular action, and Poncet mentions a case of rupture of a fatty heart in an alcoholic subject.

The reader must not gain the impression that the patient tosses wildly about in bed: on the contrary, he keeps as still as possible, and such a patient might easily be passed in the ward without appreciating the fact that he was the victim of so terrible a disease. On closer inspection, however, he will be found lying upon his side, with his head drawn rigidly backward and with a deep hollow in the curve of the spine, which curvature becomes greatly exaggerated on turning down the bed-clothes. His mind is perfectly clear, but the rigidity of the muscular contractions of the mouth and in the chest does not enable him to emit more than muffled groans. The spasm of the sphincters renders movements of the bowels or of the bladder very difficult. There is at this time but little fever; the temperature-curve is in no way characteristic in this disease, but as death approaches, and even post-mortem, the rise may be excessive. There will be found, however, after each convulsion a tendency to perspiration, which may become quite a characteristic feature of the case. With each active and extensive innervation of muscular fibres there is without doubt an increased heat-production, and the diaphoresis is therefore a means by which a corresponding heat-elimination may be maintained. The post-mortem hyperpyrexia which is occasionally seen, the thermometer running to 109°, 112°, and 113° F., may be in part due to the cessation of active heat-elimination, but it is probably due also to the action of the ptomaïne on the thermic centres.

During the height of the disease—that is, on the third or the fourth day—exhaustion becomes marked from loss of nourishment and of sleep. Short periods of sleep may be obtained by drugs, during which there is some relaxation of the muscular spasm; but no complete remission ever occurs, and the patient is soon startled out of a disturbed slumber by renewed convulsive movements. Attempts to give food may bring on spasm of the glottis, death having occurred during such a crisis. Attempts to expectorate the accumulated mucus may also produce the spasm. The convulsion usually lasts a few seconds only, during which there is also cyanosis of the face and its muscles are contracted; the pupils are normal; there is some foaming at the mouth; and the lips have a deeper hue. Dyspnœa is increased, and the patient makes forcible attempts to get his breath; the abdomen is pushed forward, and the patient may rest upon his occiput and heels in the position of opisthotonos. The pulse is greatly accelerated, and it may reach to 160 (Poncet). Death from heart failure may also occur during this period of prostration. In the last stages of the disease the mind continues clear, delirium is extremely rare, and the patient is fully sensible of the agonizing spasms to which the slightest noise or disturbance in the room gives rise. The face is pale and emaciated, and if not convulsed there is an expression of great apprehension. The voice is feeble and the skin is constantly bathed in sweat. It is in this period that the temperature may rise, and in some cases may reach a very high point. During the last moments the tetanic spasms may relax, but they are usually maintained until the end.

In tropical climates the period of acute tetanus may greatly be shortened, and cases are reported in which death has supervened a few hours after the onset of the attack.

Contraction of the muscles of one side of the trunk may occur occasionally, but pleurosthotonos is rare. When the symptoms are continued beyond the fifth day, there is hope that the disease may assume the form known as *chronic* tetanus. The cases of recovery from acute tetanus that occasionally occur usually go through a chronic stage before convalescence takes place.

In *chronic tetanus* the first symptoms usually appear at a later date after the injury or operation than in acute tetanus. There is hope, therefore, if no symptoms are seen until the third week, that there may be this type to deal with. The order in which symptoms appear is the same as that in the acute form. The stiff neck, the locked jaws, and the rigidity of the muscles of the trunk are all present, and they may be of great severity; but, although the development of the disease may be rapid, there are periods during which the patient experiences relief from muscular contractions. An entire day may pass without relapse. The periods of quiescence between convulsions may, at all events, be more prolonged than those in the acute type; nourishment can be given, and the strength of the patient may correspondingly be maintained. As time passes the interval between the convulsive seizures becomes more prolonged and the convulsions are less severe; deglutition becomes less painful. The prostration, however, is extreme, and any unusual excitement or irritation, such as the passage of the bougie, will bring back the spasms. Sleep, however, becomes more prolonged and more refreshing. Convalescence finally sets in, though it is liable to be accompanied with several relapses. The disease may be thus extended over a considerable length of time. Cases of six weeks' and of two months' duration are occasionally seen; Yandell reports one case in which the duration of symptoms was two hundred and forty days.

Head Tetanus, or Tetanus Hydrophobicus, an affection first described by Rose, occurs after injuries in the region of distribution of any of the twelve cranial nerves; consequently it is chiefly confined to the head. It is characterized by spasm of the pharyngeal muscles and paralysis of the facial nerve, as well as trismus, and occasionally tetanic contractions of the muscles of the neck and abdomen. Rose explains the paralysis of the facial nerve by compression in the petrous portion of the temporal bone, due to swelling of the nerve. According to Brunner, the reported symptom of facial paralysis is due to an error of observation. Brunner injected pure cultures of the tetanus bacillus at different points on the heads of rabbits and guinea-pigs, and succeeded in producing head tetanus. Paralysis of the affected side of the face was, however, absent. The asymmetry of the two halves of the face was caused by tetanic contractions. If the injection was made in the median line, both sides of the face were affected; if one side was inoculated and the facial nerve of the same side divided at the same time, the contractions of the muscles were prevented. Klemm by a careful analysis of twenty cases disproves Brunner's theory, it being evident that paralysis of the facial nerve occurs in the majority of cases with its characteristic symptoms. The sequence of symptoms in this form of tetanus resembles that described by Rosenbach in tetanus produced experimentally in animals, in whom the muscular cramp begins at the point of inoculation and spreads to other muscles. The paralysis is due to infection, probably by a toxine, in the same way that paralysis occurs in diphtheria and other infectious diseases. Albert, in fact, places this affection in the class of the *paralysies infectieuses.*

Cephalic tetanus occurs usually after a wound in the face. Rose reports the case of a coachman who received a blow from a whip-handle below the left orbit. In another case a blow was received in the temple during a street-brawl, and the patient was left unconscious in the gutter for several hours. In a case reported by Bernhardt the disease followed the removal of a wen from the neighborhood of the left orbit. The paralysis of the facial nerve almost always occurs on the same side as that on which the injury is received. There is usually marked paralysis of the lower lid, the eye of the affected side remaining open after an attempt is made to close the lids. There is generally trismus, and occasionally spasm of the abdominal muscles is also mentioned. A marked feature of this form of tetanus is difficulty in swallowing, which symptom has given rise to the term *tetanus hydrophobicus.* This symptom, however, is not always present.

Head tetanus is not always fatal. As in the ordinary form of tetanus, many of the chronic cases recover. Gueterbock and Bernhardt collected seventeen cases with four recoveries. Klemm found that recoveries occurred almost invariably in the chronic cases, which lasted from four to twelve weeks. In a collection of twenty-four cases of head tetanus seven recovered, and of these six were cases of chronic tetanus.

As to the *character of the wound* in a case of tetanus, there is little to show that the bacilli produce any marked local effect during their growth. Poncet speaks, however, of a peculiar condition of the wound at the outbreak of the disease. The suppurative process is less healthy in character and the tissues appear to be irritated. Occasionally there is a slight blush around the edges of the wound, and sometimes evidences of lymphangitis are seen near a wound of the extremity. There may also be a slight pricking sensation in the affected member, which may even be painful.

Wounds of the extremities are said to be followed more frequently by tetanus than those in other regions. This statement is in accord with Yandell's figures. He says: "The popular belief that injuries of the foot are more liable than those of other parts to be followed by tetanus is quite confirmed as to punctured wounds in this situation, the large majority being inflicted by nails run into the foot." Of the 505 cases reported in the Surgical History of the War, all but 76 were wounds of the extremities. It is probable, however, that the nature of the injury is a more important etiological factor than is its situation, and that tetanus more frequently follows wounds of the extremities is due to the fact that punctured wounds are more frequent in those regions. The presence of the bacillus tetani on dirty hands and feet may also form an important factor. Occasionally the disease will be found to follow the infliction of a certain kind of injury. The "deadly toy pistol," so well known to Fourth-of-July celebrations, has been responsible for many cases. Here it would seem that there is a combination of predisposing causes—youth, anatomical situation, a lacerated or a penetrating wound, dirt from the street, and finally fragments of gravel from the detonating composition. The presence of foreign bodies in wounds has always been supposed to be a frequent cause of tetanus. The wound, however, may be extremely slight, as a contused wound of the toe with or without fracture, a trivial affair; but if the bacillus has found a suitable lodging and is well protected from oxygen, the development of the organism will be possible. The penetrating nature of gunshot wounds, such as are inflicted in battle, combined with certain predisposing causes, explains the relative frequency of tetanus in military surgery. That there should be a certain amount of inflammatory reaction in the wound is to be expected when infection has taken place; but the moderate number of organisms found probably accounts for the fact that more marked symptoms of inflammation are not present. The existence of such symptoms of a septic inflammation as Poncet describes can probably be accounted for by a mixed infection.

The testimony as to the *post-mortem changes* in tetanus is quite conflicting. As a rule, evidence of inflammation of the brain and its meninges is wanting, but a number of observations point to inflammation in the upper portions of the cord. The great difficulty in preparing so delicate structures for microscopical study throws doubt on many of the reports, but enough remains to prove that inflammation of nerve-tissue, both central and peripheral, is generally present. Doubtless a fresh study of the field in the light of the present bacteriological knowledge will bring out many interesting morbid changes hitherto unobserved.

Larrey, after the battle of Waterloo, performed a great number of autopsies in cases of tetanus, and found evident traces of inflammation of the cord and the membranes. Grinelle (1857), in a summary of 52 cases of tetanus, reports that 29 presented lesions of the cord and the membranes. In 3 changes were noticed in the brain, and in 11 in the nerves and muscles. Lockhart Clarke, the best authority of the time, found in six cases lesions of the cord of different kinds and of surprising extent. He says: "It seems to consist precisely of disintegration and softening of a portion of the gray substance of the cord, which appeared in certain parts to be in a state of solution."

Ranvier, however, examined four cases from four to twelve hours after death, and prepared the cords for microscopical examination with the greatest care, but failed to find anything abnormal. Verneuil believes that the lesions are dependent entirely upon reflex action, and Brown-Séquard expresses the theory that the morbid changes are due to an ascending neuritis; and indeed in many cases there is a redness of the neurilemma of the nerves corresponding to the locality of the wound. Both Michaud and Aufrecht found lesions in the lumbar portions of the cord. Laveran examined the nerves of a patient who died of tetanus following amputation of the leg. He found proliferation of connective tissue in the tibial nerve, but no changes in the cord.

In America, Amidon claims to have found extensive changes in the nervous system; small thrombi and exudation in the dura mater; degenerative changes in the brain; evidences of inflammatory changes at the points of origin of the cerebro-spinal nerves; and lesions in the cord. Jewell thinks there is little doubt that there is usually irritative disease in certain not very well defined tracts of the gray matter of the spinal cord and the medulla oblongata, more especially of the latter. "From these central diseased parts excitations are propagated along the motor tract, down the medulla and cord, and thence along the motor nerves to the affected muscles." In the spinal cord the chief seat of the disorder, he thinks, appears to be in the posterior cornua and the contiguous central gray matter, the disease at times invading the related white columns. Such changes are more frequent in the cervical portion, but the appearances observed depend greatly upon the duration of the case. Neither the motor nor the sensory tracts are invaded alone, but the precise point of irritation appears to be in an intermediate region through which transfers in reflex action are made, and there is consequently great exaltation in the reflex irritability in this disease.

This brief review of the question is enough to satisfy one that the virus acts with more or less power chiefly upon the nervous centres of the cord and the medulla, but the data do not yet seem to be sufficient to establish the fact of multiple neuritis or irritation of the trunks or branches of the nerves over and above that of other tissues to which the virus may be conveyed.

The *diagnosis* of tetanus is usually not difficult in the fully-developed stage of the disease, but it is in the earliest stages that the surgeon should be warned of what is about to come. Stiffness of the jaws may be due to inflammatory affections of the mouth or the teeth or to abscess of the cervical glands. When the external signs of inflammation are wanting, the latter source of disturbance might be overlooked.

Rheumatic inflammation of the temporo-maxillary articulation may also prevent the patient from opening his mouth, but the signs of local inflammation are not difficult to discover if carefully sought. Hysterical contraction of the masseter muscles is not likely to give rise to a mistake in the diagnosis, for the surgeon's attention is not usually called to such a condition until time has long since solved the question. Colles of Dublin undertook to describe the different forms of reflex contractions which may be mistaken for tetanus. Temporary spasms following the dressing of a painful wound mentioned by him would not probably lead to a mistake in diagnosis. Tetanic spasms due to peripheral irritation of the nervous system, such as by a scar or a foreign body, are at times severe, and, according to some authors, may be fatal. Some of these cases are probably true infective tetanus; others may be examples of severe reflex irritation, and Larrey's case of sudden cure following the division of a scar may have been one of this type.

The question of death by tetanus or by strychnia-poisoning has been raised in medico-legal cases. In the latter condition, however, there is usually no lock-jaw, and if the masseters are affected at all, it is toward the end of the scene. In strychnia-poisoning there is hyperæsthesia of the retina and objects seen are colored green. During a paroxysm the mouth foams, the jaws are joined together, and the teeth lacerate the tongue. There is also spasm of the muscles of the limbs and body, with arching of the back, which symptoms with laryngismus are first in order to appear. When the dose is small and is repeated, there will be a corresponding intermission and a return of all the symptoms. In tetanus the disease begins with mild symptoms, and it is progressive and continuous. In acute poisoning the symptoms may last only for a few minutes. In temperate climates the most acute forms of tetanus last from two to three days.

Tetany, which it might be supposed would resemble tetanus, is a disease not often seen in America: it affects chiefly young persons, and consists in tonic spasms of various groups of muscles, most frequently those of the upper extremities. The attack is preceded by vague tingling pains, followed by a sense of stiffness in the affected group. The position of the hand during the spasm is peculiar, resembling the posture of the accoucher's hand when about to make a vaginal examination. Opisthotonos may occur, but there is never trismus. The attacks are short and are more or less localized, and Trousseau's symptom, seen in no other convulsive disease, is always present. This symptom consists in the peculiarity that pressure upon the nerve-trunk leading to the affected group of muscles always brings on a characteristic attack.

The febrile nature of meningitis and the frequency with which it is accompanied by pain in the back of the head, as well as by the absence of the great reflex excitability, serve to distinguish that affection from tetanus.

Hydrophobia is supposed by some authors to resemble tetanus, owing to the difficulty of swallowing which occasionally arises in the latter disease. Any one who has once seen both diseases would find no difficulty in distinguishing them. The portraits of the two diseases are indeed strikingly different. The countenance and bearing of the hydrophobic patient are those of excitement and mental distress. In the early stages of hydrophobia the patient does not take to his bed, and the so-called "spasm" appears only on attempting to swallow, and it is limited to the muscles of deglutition and respiration. The facial paralysis is a sufficient guide to diagnosis in tetanus hydrophobicus, where there is difficulty in deglutition. External muscular spasm is the characteristic feature of tetanus. There is no mental excitement; although the muscles of the face are distorted, the expression of the eye is natural. It is the endeavor of the tetanic patient to keep as still as possible, whereas the hydrophobic patient is constantly moving about. In the later stages mania is present in hydrophobia, but in tetanus the mind is clear to the last.

The *prognosis* of tetanus depends almost entirely upon the acuteness of the symptoms. Acute tetanus is one of the most fatal of diseases. In chronic tetanus the percentage of mortality is very much lower. According to Hippocrates, the patient dies on the third, the fifth, the seventh, or the fourteenth day. If he survive this period he recovers. According to the tables of the Surgical History of the War, of 337 deaths, 287 occurred during the first week of the disease. On the eighth day there were but 7 deaths. In Yandell's 415 cases there is a marked falling off in deaths on the fifth day, when there were but 11 deaths, from which time the percentage steadily diminished.

Traumatic tetanus appears to be more fatal than idiopathic tetanus. Those cases occurring after injury received upon the field of battle appear to be the most fatal of all. In the Civil War 505 cases are recorded, of which 451, or 89.3 per cent., died.

Poncet found a mortality of 90.6 in 713 cases; of Yandell's cases, which were collected from various sources, 213 recovered and 182 died.

The *date of invasion* of the disease is an important element in the prognosis. In Yandell's cases the disease supervened in two weeks after the injury in 196 cases: of these, 62.5 per cent. died. "But when tetanic symptoms are delayed until the fourteenth day recoveries are notably in excess of deaths—23 per cent." Tetanus is seen more frequently in the male sex, and it is a disease of early life: cases are rarely seen in patients over fifty years of age. The gravity of the wound does not appear to have any influence upon the severity of the disease. It must not be forgotten that the figures mentioned above do not take into consideration tetanus of the tropics. There the disease is not only much more fatal, but is also much more frequent. According to Poncet, the number of deaths from tetanus in England amounts to 0.0031 of the total mortality, but in Bombay the figures rises to 3.9 per cent. The disease in that locality may prove fatal in a few hours after the most trivial injuries or even when produced by a sudden chill.

The *treatment* of few diseases has been the object of such varied medication as tetanus. Not only is the number of remedies too great to attempt even an enumeration, but such a variety is also used in most cases as to render it difficult to judge of their respective values.

Yandell, after a careful study of this question, concludes that no one agent can justly be said to possess a decided superiority over any other. No attempt is made to draw any conclusions from the treatment employed in the cases which occurred during the Civil War. Yandell places chloroform at the head of the list in cases of acute tetanus, but also makes the significant statement that when tetanus continues fourteen days recovery is the rule and death the exception, apparently independent of the treatment.

Among the internal remedies which have enjoyed a more than usual reputation may be mentioned Calabar bean, chloral, cannabis indica, curare, nitrite of amyl, quinine, and opium. Calabar bean, or its active principle, when given in small doses, relieves the muscular contraction, the jaws relax, the head reposes quietly upon the pillow; if given in large doses, the spasm appears greatly aggravated. Poncet explains the favorable action of the drug by its effect upon the conductibility of the motor nerves, by which the muscular system is, as it were, isolated from the nerve-centres. He prefers to give it by the mouth rather than by subcutaneous injection, as the dose can more carefully be regulated and the action of the drug can better be observed by this method. From 1 to 1½ grains of the extract may be given by the mouth every four hours, or from 15 to 20 drops of a 1 per cent. solution may be injected subcutaneously. The statistics of Knecht give a mortality of 45 per cent. in 60 cases in which this drug was used.

Chloral seems to be most efficacious in chronic tetanus: it relieves pain and prevents spreading of the muscular spasm and recurrence of the convulsions. It appears to act by diminishing reflex excitability in the nerve-centres. It may be continued for one or two weeks at a time, and in this way an almost uninterrupted sleep may be maintained, which paves the way to convalescence. In large doses (from 100 to 200 grains a day) chloral will relieve muscular spasm in acute tetanus, but it does not appear to have any appreciable effect upon the mortality. According to Jewell, as much as 1120 grains have been given in twenty-four hours.

Oré of Bordeaux cured one of his patients by the intravenous injection of chloral: 10 grammes of chloral dissolved in 20 grammes of water were injected into the right cephalic vein in the space of nine minutes; cyanosis disappeared at once, and all muscular contraction ceased at the end of the operation; the patient fell into a quiet sleep. The relief was in another case only temporary, and in fifteen minutes the symptoms had returned.

Chloroform may be administered by inhalation. Poncet relates a case where anæsthesia was produced six times, and at the last administration respiration suddenly ceased, but it was restored by artificial means, and the patient finally recovered under the continuous treatment of opium. Simourin administered chloroform by keeping upon the breast of the patient a napkin upon which chloroform was dropped. The room was a small one, and the patient was thus exposed to the influence of the drug during twenty-two days. The patient recovered. Certain it is that the weight of evidence is in favor of the sedative action of this drug on the nervous system in cases of tetanus, as compared with that of other remedies of this class. Its action is said to be not so enduring as that of chloral.

Opium does not appear to enjoy the popularity of chloral and chloroform. Large doses are required, and the digestive disturbance caused by the drug is a contraindication to its use. Administered hypodermically, it gives, however, great relief in some cases. The dose required is sometimes enormous, considering that the patient has but a short time to become habituated to the drug. The writer has known a young man to receive, before relief from pain was obtained, one hundred grains of morphine in the twenty-four hours.

Bromide of potassium may be used in connection with chloral or, in the convalescent stage, as a substitute for that drug, but it is altogether too mild a remedy to produce any appreciable effect in the more active stages of the disease. The writer should hardly advise the surgeon to waste time in experimenting with any of the other drugs that have been used in the treatment of the disease. Those already mentioned are of use only by virtue of their sedative qualities, and they cannot be regarded as curative agents. They relieve the most overpowering of the symptoms, and in this way give the patient strength to live through the period during which the virus is in an active stage of development.

So far as local treatment is concerned, it is important to remember that antiseptics, to be of any use, must reach the bacilli, which are already deeply imbedded in the recesses of a punctured wound. Those exposed to the air, being anaërobic, are not likely to develop. Punctured wounds, therefore, should thoroughly be laid open and disinfected if there is any reason to suspect that infection has taken place. This infection is more likely to occur, as has already been shown, when dirt or dust is driven in with the penetrating foreign body. The large majority of punctured wounds recorded in Yandell's cases were inflicted by nails penetrating the foot. Any dressing applied should be so arranged that free drainage will be possible. A dry dressing, which might seal up a small opening, would in such case become a source of danger. Many a case of tetanus has doubtless been warded off in pre-antiseptic days by an old-fashioned poultice, which has favored suppuration and the discharge of the dangerous bacilli. In those cases to which attention has already been called, where nerve-irritation is a prominent feature, the reflex excitability has been greatly diminished by nerve-section. Some cases seem to have been cured by this operation, but in true tetanus the most that can be expected from this method is the removal of a powerfully disturbing influence on the nerve-centres. Permanent paralysis may of course result, but union may subsequently take place between the divided ends of the nerve. Nerve-stretching has also been tried, but the results have not been encouraging, although in isolated cases it has produced marked relief. Nerve-stretching is not to be thought of except in special cases when local indications seem to demand this operation. When a nerve is bound down by a cicatrix, it should be dissected out and thus be freed from a source of painful irritation. In certain cases when the wound is foul or is irritating, or when great laceration has exposed and mangled nerve-trunks, amputation may be necessary.

The great sweating which is so characteristic of tetanus has suggested the use of warm baths and of other diaphoretics as a means of imitating Nature's method of relief. It is possible that some of the ptomaïnes may be eliminated in this way: it is unlikely that many of the bacilli would find their way into the sweat-glands, as bacteria are not usually so eliminated. The hot bath gives relief to the spasms while the patient is immersed, but removal from the bath brings the patient in contact with cooler media, which, together with the necessary disturbance, excite new convulsive movements. A *vapor bath* may be administered to the patient while in bed. The vapor bath constitutes one of the classical forms of treatment handed down from early times. The writer has seen it thoroughly tried without other result than to increase the patient's distress.

In 1890, Behring and Kitasato published some experiments with reference to the origin in animals of immunity to diphtheria and tetanus. According to these investigators, the acquired immunity depended upon some property of the blood-serum developed by protective inoculations, and with this curative serum they were not only able to render animals insusceptible, but also to cure already infected animals. This immunity was brought about by the injection of cultures of the tetanus bacillus, whose activity had partially been destroyed by the addition of trichloride of iodine. By diminishing the amount of the iodine the strength of the virulent culture could be increased. The serum of animals thus rendered immune could be used on other animals as a protective or curative agent. Tizzoni and Catani produced a protective result in animals by injecting very small doses of tetanus culture at first, and later by gradually increasing the amount of the culture. They were not able, however, to produce any therapeutic results on animals with the serum of the animals so treated. The active principle of the culture they called a "tetanus antitoxine," which may be obtained by precipitation by alcohol, and when used it is dissolved in water or in glycerin. (See Appendix.) The curative effect of this blood-serum does not seem to have proved so powerful as was at first anticipated, and it is denied altogether by some observers. Other observers have succeeded, however, in curing animals when the treatment was begun soon after the onset of the symptoms of tetanus.

Fourteen cases of the disease in man have been treated by the methods of Tizzoni and Catani; of these, ten were adults, who were all cured. There were four cases of tetanus neonatorum, three of which terminated fatally. This method consisted in injecting a watery solution of the antitoxine and in repeating the dose daily. No unfavorable symptoms followed the administration of these doses in any of the cases. An analysis of the favorable cases shows, however, that the majority of them were examples of chronic tetanus. The cases reported by Roux and Vaillard were also mild in type. It is therefore doubtful whether this new treatment is efficient in the acute type of the disease.

Perhaps in no disease should the comfort of the patient so carefully be studied. Before active symptoms have set in the patient should be placed alone in a room so situated as to be quite free from disturbance of any kind, if that be possible. The light should be dim and the temperature should carefully be regulated. Officious nursing should be avoided. Nourishment is needed to sustain strength, and stimulants may be given in such combinations as to be least irritating to the throat. It may be necessary to use the catheter or to produce an action of the bowels. Skilled nursing should accomplish these tasks without undue excitement of the hyperæsthetic nerves. With such minute care and attention to details as these rules imply treatment may, as Nicaise justly says, make chronic some cases of tetanus that began as acute. Every day added to the patient's life after the first week of the disease increases greatly his chances of recovery. Even the most acute cases sometimes get well, so that the surgeon should be encouraged to exert all the skill in his power or bring to bear all the resources of a great hospital, even in the most desperate cases, with some hope of saving life.

XIX. HYDROPHOBIA.

HYDROPHOBIA is a disease of man caused by inoculation from a rabid animal due to a specific virus in the saliva. Hydrophobia, which principally affects the nervous system, is characterized by peculiar paroxysms of suffocation, brought on chiefly by attempts at swallowing, by a catarrhal affection of the fauces, by a more or less pronounced febrile disturbance, and by an acute mania. The term *rabies*—or less frequently *lyssa*—is applied to the same disease in animals.

Rabies is frequently observed in herbivorous animals, such as the ox, the horse, or the sheep. It is more commonly found in the carnivora, such as the cat, the fox, the jackal, the wolf, and the dog. More rarely it is observed in the skunk, in swine, in birds, and even in domestic poultry. Rabbits are susceptible to the virus, and they are used principally in experimental inoculations. The disease is always communicated by inoculation from animal to animal or from animal to man, and does not arise *de novo.*

Infection does not always follow the bite of a rabid animal: the large majority of persons bitten are supposed to escape, but in most cases this immunity is due to protection by the clothing or the failure to penetrate the epidermis, or, more probably still, to the fact that the supposed rabid animal did not suffer from rabies. Bites on exposed portions of the body by animals undoubtedly mad are probably followed by hydrophobia in the large majority of cases. The disease is not always caused by a bite, for a previously existing wound or an abrasion may be inoculated by the saliva conveyed by the tongue of the animal while licking the skin of its master.

In the dog the disease presents two types, the dumb and the furious rabies. In the *furious form* a change is first noted in the habits of the animal. He becomes uneasy and depressed, and is dull, wandering aimlessly about and hiding in obscure corners. In this early stage his saliva is already poisonous, and, as he occasionally exhibits a tendency to be affectionate to some other animal of the household or to his master, his caresses are dangerous. Frequently, however, if disturbed, he growls and shows no inclination to move, but will still obey the voice of his master. He is subject to hallucinations, and will snap and snarl at imaginary objects.

Doléris mentions the case of a bull-terrier which was observed to peck, like a hen, at the hay scattered about the floor of the stable when there were no other symptoms. He was isolated and died of rabies. The symptom of hydrophobia does not exist in the dog: on the contrary, the dry and swollen state of the mucous membrane of the fauces causes him to seek water to slake his thirst. The animal will plunge eagerly into the water and bury his head beneath it to relieve this symptom. Rabid animals have been known to swim a stream to attack animals on the opposite bank.

At first the dog takes his nourishment as usual, but he soon becomes voracious in his appetite, and in intense forms of the disease he often exhibits a depraved taste, avoiding ordinary food, but tearing all kinds of objects and swallowing the fragments. He may even swallow his own excrement. The quantity of the saliva is not great at first, but it is more abundant in the earlier stages than later. It then becomes tenacious, adhering to the gums, and appears almost as white as snow. The dog's bark is quite characteristic: it is at first husky, and in some cases ends in a plaintive howl somewhat like that of a dog barking at the moon. The sight of another dog generally brings on a paroxysm of rage—a symptom sufficiently marked and constant to be of value in cases of doubtful diagnosis. The affected brute will pass by other animals and man to attack another dog. He is usually quite insensible to pain: a red-hot poker may be grasped and held in the mouth. He can be beaten without exhibiting signs of pain, and often commits self-inflicted wounds. There may be great sensitiveness of the scar of his cicatrized wound.

As the disease progresses there is marked inability to swallow either fluids or solids, and loss of strength is often progressive and rapid. The respiration is hurried. During the later periods of the disease delirium becomes a marked symptom. The animal is now seized with a desire to escape from the house, and it is during this stage that he becomes dangerous. His pupils are dilated, and his expression is terrible in its fierceness. He now attacks all animals within reach, and also man. While biting and tearing he is, according to Suzor, always silent; unlike the non-rabid dog, which fights and barks at the same time. This stage is followed by one of great prostration. His gait is now tottering and his senses are dulled. After wandering about for a few hours, or it may be days, paralysis of the hind-quarters supervenes, and he dies of exhaustion and asphyxia. The disease usually lasts from six to eight days, but it may be prolonged for several days.

The *period of incubation* of rabies varies from three to four weeks. It is occasionally very much longer. In nearly every case the disease terminates fatally.

Dumb rabies is commoner than the furious form. The initial symptoms closely resemble those of furious rabies. The voice in dumb rabies is much altered from the first, and in the later stages it is lost. The expression is sad and startled: the mouth is open, owing to the paralysis of the lower jaw, and the tongue hangs out dry and discolored and covered with dirt. Persons not acquainted with these symptoms might suppose the animal to be suffering from a bone lodged in the throat, and would, in making efforts to remove it, certainly expose themselves to inoculation. Paralysis of the hinder extremities supervenes, and it is soon followed by death. The symptoms in rabies appear to vary according to the regions of the cord which may be chiefly affected.

On *post-mortem examination* the mucous membrane of the mouth and the tongue is found to be of a livid color. Ulcerations of the mucous membrane, supposed to be due to vesicles characteristic of the disease, are frequently caused by the swallowing of foreign bodies of various kinds, such as stones, straw, hair, and glass, with which the stomach is found to be filled. There is great congestion of the tracheal and bronchial mucous membranes, and there is a marked contraction of the bladder. Congestion of the central nervous system is also found.

The *etiology of hydrophobia in man* is not yet fully explained. Pasteur has been unable to demonstrate any form of bacteria which can be identified with the disease. Fol and Rivolta have lately described a coccus in this disease, but their observations have not been confirmed by others. The virus is probably never absorbed through the mucous membrane: Doléris mentions cases of persons who had eaten with impunity the flesh of rabid animals. The bites of certain species are said to be more dangerous than those of other animals. In Russia it is believed that wolves are more dangerous than any other animals, and in America the bite of the skunk is greatly dreaded. There is probably no difference in the strength of the virus in these animals, the more frequent poisoning being probably due to their sharp teeth and to the greater certainty of inoculation through the penetrated skin.

The period of the year is supposed to exert a favorable influence upon the development of an epidemic of hydrophobia. The results of the work of Pasteur's Institute show that the disease is not confined to any one period of the year, and that, contrary to the common belief, it is not a disease of the summer months. Two at least out of four cases which have come under the writer's observation occurred during the summer. Pasca of Milan found the disease occurred more frequently during the spring and autumn months.

The *period of incubation* of the disease in man is quite variable, although the first symptoms usually make their appearance in the second month after exposure. According to Brouardel, the disease rarely occurs after the third month, and quite exceptionally after the sixth month. The symptoms manifest themselves earlier when the bites are numerous and severe, and they appear also earlier in children than in old people. Cases are quoted where the disease is said to have supervened several years after infection, but the extension of the period of incubation beyond those above named is to be received with caution.

The disease appears to be very much commoner in France than in America. Further reference will be made later to the number of cases occurring in France. In the city of New York there were, during a period of thirty-five years, only 76 deaths from hydrophobia. In 9 of these years there were no deaths, and it has twice happened that for two years in succession there was not a death. In Boston and its vicinity H. C. Ernst reports an epidemic of rabies among dogs during 1889 and 1890, some 60 cases being observed at the Harvard Veterinary Hospital. During the summer of 1890, 3 cases in man were observed at the Boston City Hospital, from 2 of which material was taken by Ernst and successfully inoculated into rabbits, which died with the usual symptoms.

The disease may appear either as a delirious or as a paralytic form, precisely as in the dog, but the delirious form is the variety by far the most frequently observed.

The first stage of the disease is characterized by melancholia. It is marked by insomnia, by loss of appetite, and by great depression of spirits, and occasionally there are shooting pains found radiating from the seat of the wound or in the affected limb. In a case reported by Shattuck the patient first complained of severe pain in the back of the head and in the neck; on the next day he went as usual to his business, but he returned home at an early hour much depressed, saying, "I have come home to die." Difficulty of swallowing appeared on the same day. This stage does not last more than twenty-four or forty-eight hours, although some authors have described cases in which headache, insomnia, and anorexia were observed for three weeks previous to the outbreak of hydrophobia.

The cases seen by the writer had all reached the stage when that most striking symptom of the disease—difficulty in swallowing—was plainly marked. The appearance of the patient at this time, although not presenting symptoms likely to attract the attention of the casual observer, is most characteristic. The picture thus presented is one not likely to be forgotten or to be mistaken for any other disease. On entering the apartment one looks around involuntarily to find the patient, for the individual, quietly seated with his back partly turned to one, is dressed in his ordinary clothing and gives no indication of suffering from any abnormal condition. A brief conversation, however, soon brings out the peculiarities of the case. His speech is perhaps the first function to betray the disease. The patient appears to be slightly out of breath, frequent short inspirations so altering his conversation as to give to it the so-called "sobbing" tone. It is, indeed, not unlike the speech of a child who has recently been crying and is endeavoring to control itself. The expression of the face at this time varies from one in no wise differing from a perfectly normal condition to a more or less wild or a haggard look about the eyes. Usually there is an appearance of depression or of anxiety, like that of a prisoner waiting for the verdict. But the most crucial diagnostic test is the glass of water.

The following account of the attempts made by a patient to drink is given by Curtis, with whom the writer saw the case in consultation:

"A glass of water was offered to the patient, which he refused to take, saying that he could not stand so much as that, but would take it up from a teaspoon. On taking the water in the spoon he evinced some discomfort and agitation, but continued to raise the spoon. As it came within a foot of his lips he began to gasp violently, his features worked, and his hand shook. He finally almost tossed the water into his mouth, losing the greater part of it, and staggered about the room, gasping and groaning. The respiration seemed at this moment wholly costal, and was performed with great effort, the elbows being jerked upward with every inspiration. The paroxysm lasted about half a minute. The act of swallowing did not appear to distress him, for he could go through the motions of deglutition without any trouble. The approach of liquid to his mouth, however, would at once cause distress."

It will be noticed that the "spasm," as it is called, does not involve the muscles of the pharynx and the œsophagus, but affects rather the mechanism of the respiratory apparatus. It is true that many authors report spasms of the muscles of the pharynx, and even of the jaws and the extremities, but these are secondary to the overpowering sense of suffocation. The palpitations of the heart are also violent, and the cardiac disturbance has been described by Doléris as a *spasme circulatoire*. Of the nature of the hydrophobic paroxysm something further will presently be said.

Distress is also caused by fanning the patient or by exposing him to a draught of air (*aërophobia*). In one case, on gently passing the fan to and fro behind the patient's head while other persons were conversing with him, the writer produced a disturbance sufficient to cause the patient to spring from his chair and to walk rapidly to the other side of the room. The patient did not appear, however, to be conscious of what had disturbed him. In another case, a lump of ice being placed in the patient's hand, he flung it from him with expression of great pain; on being asked what his sensations were, he explained that it felt like a red-hot coal.

Already at the end of the first day the mental condition of the patient is evidently impaired, the expression of the eye has grown more wild, and the speech has begun to be somewhat incoherent. Cephalalgia is a frequent symptom, and it is occasionally of great intensity. In one of the paroxysms of the case already referred to the patient would exclaim, "For God's sake, hold my head or it will burst!"

There is at this time a secretion of viscid saliva, which can be seen accumulating about the teeth and the lips. The irritation of the fauces is great, and in the effort to expel from them the adherent secretions there is developed a loud and abrupt cough, which has probably given rise to the tradition that such patients "bark like a dog."

Presently the paroxysms appear to come on spontaneously. The patient, who by this time has become fatigued by the nervous excitement, by the exhausting paroxysm, and by the inability to take food, has been persuaded to go to bed. The accumulation of saliva causes attempts to swallow or to expectorate, and the contact of the secretions with the fauces or with the lips causes irritation sufficient to bring on an attack. The paroxysms are doubtless caused also by mental apprehension of an impending attack. On the approach of the paroxysm the patient, who a moment before has been quietly lying in bed, may suddenly spring out of bed and grovel on his hands and knees in a distant corner of the room. Violent attempts at expectoration may occur. At this stage of the disease there will probably be more or less marked mental disturbance. The patient's opinion of the manner in which he has passed the night is quite unreliable. Acute mania may supervene, and in one of the cases which the writer saw the patient escaped from his room early in the morning, and was found to have scaled a high fence and to have concealed himself at some distance from the hospital. Marked sexual excitement is frequently observed: in men the talk is obscene and painful emissions may occur; in women nymphomania may be present. During the period of mental excitement the patient may struggle fiercely with his attendants. Occasionally he may attempt to bite, but this is in no way characteristic of his condition. In some cases during this stage melancholia is present in a marked degree: the patients are the prey of nameless terrors, and many cases of suicide are recorded.

After each paroxysm prostration becomes more marked, and in some cases coma may supervene temporarily. At the end of the second day, usually, the prostration is so great that the attacks are much feebler, and toward the close of the scene the patient may become comparatively quiet. The transition from prostration to coma is rapid, and the moribund stage is usually short. Febrile disturbance does not appear to be a marked feature, although occasionally it may appear with the outbreak of the disease; but pyrexia is present in the later stages, and in one case which the writer saw the temperature ran above 104° F. on the last day. The pulse usually is not greatly accelerated.

There may also be a *paralytic form* of rabies in man, although this form is much rarer than is the furious form. Gamaleia of Odessa published an account of thirty cases. He found that the disease is the result of deep and multiple bites. At the onset there is considerable fever, malaise, headache, and vomiting. There is also pain in the extremities, particularly in the part bitten. Paresis and numbness appear in the group of muscles near the injured parts, these disturbances being followed by more or less complete paralysis. The paralysis then spreads, preceded or accompanied by sharp pain in the muscles invaded; the remaining limbs, the trunk, the rectum and the bladder, the face, the tongue, and the eyes, are all paralyzed, and finally there is paralysis of the respiratory centre, with more or less difficulty in swallowing liquids. Gamaleia says: "When well marked this respiratory lesion is the cause of dyspnœic convulsions in the muscles which are not yet paralyzed, then frequently return of breathing to the normal, but spread of the paralysis to the heart and death by syncope." This form of rabies has a duration of about one week.

Dana says: "In questioning the many general practitioners from various parts of the country with whom I come in contact, I have found that many could recall cases of mysterious acute progressive fatal paralyses whose nature and cause have completely puzzled them. It may be that the paralytic rabies in man is therefore not such an extreme rarity." Gray believes that the symptoms of the so-called "dumb rabies" may be caused by simple purulent meningitis and meningo-encephalitis.

Lyssa falsa seu nervosa, which is a term applied to a condition produced by the fear of rabies, is occasionally seen in hysterical subjects. It is not difficult to distinguish it from the true disease, as the period of incubation is too short, and a few days' or even hours' observation will decide the question, owing to the rapid development of the symptoms of true hydrophobia. Cases of lyssa falsa are said to have terminated fatally, but such a result may have been due to complications, such as an acute mania or some infectious disease. Birdsall saw a number of such cases, in none of which the patient died, but he would not say that death from fright of this kind was impossible.

According to Curtis, "the *hydrophobic paroxysm* is to be likened to the shock of the shower-bath. The regulation of the respiratory centre is accomplished by an inhibitory influence. One of the most striking examples of this action is observed in the superior laryngeal nerve. Irritation of the divided central end of this nerve causes an immediate suspension of the respiration, the diaphragm, paralyzed and relaxed, being thrown into an attitude of extreme expiration." The same result may be produced, according to Brown-Séquard, by direct irritation of certain parts of the medulla. A similar influence is exerted by a variety of peripheral stimuli: powerful excitations of the nerves of general sensation, particularly the fifth pair, cause slowing of the respiratory movements. A similar effect is produced by psychical impressions proceeding from the emotional regions of the brain and the medulla, as shown in the breathlessness experienced under circumstances of great alarm or excitement or grief. The superior laryngeal nerve supplies sensation to the mucous membrane of the base of the tongue, of the upper part of the anterior wall of the œsophagus, of the epiglottis, and the laryngeal mucous membrane. When stimulated by the irritating contact of foreign bodies, liquids, irritating vapors, and gases, paralysis of the diaphragm takes place with extreme respiratory relaxation, so that inspiration is for the time being rendered impossible. The same protective agency is brought into play in every normal act of swallowing, or even in inspiration itself, which is thus rendered, as it were, self-inhibiting.

The breathlessness in the shower-bath or in cold sea-bathing is another example of the same inhibitory action. Similar sensations are produced by the attempt to swallow a glass of hot, steaming punch, which will sometimes "take one's breath away" by the same mechanism. Swimmer's cramp is probably also another example, resulting in sudden death from apnœa, and is not due to "cramp" of the muscles, as is generally supposed.

The hydrophobic paroxysm is not to be regarded as a convulsion, unless, as Curtis graphically puts it, "a drowning man unable to swim and thrashing about in the water, or a man clutched by the throat and struggling frantically for life, can be said to have convulsions." The paroxysms are rather to be regarded as sudden attacks of paralytic apnœa due to temporary, partial, or complete inhibition of the respiratory centre taking place under the influence of peripheral impressions. The inhibitory stimulus may proceed from the area of distribution of the superior laryngeal nerve, being originated by attempts to drink and by accumulated saliva, or from the area of the fifth pair as a result of wetting the lips or the face or of fanning; or it may be due to an irritation of the nerves of sensation of the trunk and limbs or the nerves of special sense. The origin of the respiratory inhibition does not appear to Curtis to be due so much to an increase of inhibition as to diminished resistance of the respiratory centre, due to the structural changes which Gowers has shown are most intense in the respiratory centre of the medulla. All that is required, therefore, is a slight inhibitory stimulus to reduce the activity of this centre to zero. According to Putnam, it must either be assumed that the respiratory centre is abnormally susceptible to inhibitory influences or that the inhibiting impulse is extremely powerful. As the structural lesions found in the medulla show an impairment of the nutrition of the respiratory centre, the theory of over-sensitiveness to inhibitory influences must be rejected. There is no evidence that the impressions made on the skin or the mucous membrane are abnormally intensified: there is, however, the stimulus of emotional excitement which is always present in such cases. The paroxysm is therefore directly due, Putnam thinks, to the reaction on the respiratory centre of the morbid mental state of the patient.

Gowers maintains that the phenomenon is not one of inhibition, but of irritability of the respiratory centres, particularly that portion which has to do with the process of extraordinary breathing; that is, the costo-superior respiration. According to this author, the nature of the symptoms and the lesions in hydrophobia seem to suggest that *the poison has an action on the nervous centres in the following order:* the medulla oblongata, the cerebral hemispheres, and the spinal cord. The effect on the medulla is the first, the most intense, and the most constant, especially in the early stages. The action on the spinal cord is rarely marked except in the latest stage. The action on the cerebral hemisphere is chiefly shown in the delirium which is so conspicuous in some cases in the later stages.

Gowers carefully studied the microscopic condition of eight cases of hydrophobia in man and of one in a dog. The changes found in the spinal cord were comparatively slight. There was some hyperæmia of the gray substance, but no cell-infiltration. The region in which the pathological conditions were most intense is what is known as the respiratory centre of the medulla, the region in which are situated the hypoglossal, pneumogastric, and glosso-pharyngeal nuclei. Then, in addition to the great distention of the minute vessels seen in the cord, there was found an aggregation of cells in the perivascular lymph-sheaths.

The cells were found sometimes in a single layer, and sometimes so densely packed as to compress the vessel they surrounded. In some instances they had extended beyond the perivascular sheath and had infiltrated the adjacent tissues. Here and there were patches of tissue infiltrated with leucocytes in this manner. In one case such an area was found between the hypoglossal and the pneumogastric nucleus. Gowers describes them as miliary abscesses. There was also a number of small round cells scattered through the adjacent tissue in greater numbers than in health. Many vessels, especially the veins, were distended with blood-clots (showing probably the septic nature of the inflammatory stimulus). The nerve-cells presented comparatively little change: many of them had a granular appearance, which was more marked in some than in others that lay near them; others had a somewhat swollen appearance. The changes around the auditory, facial, and fifth nuclei were not so marked. The higher part of the pons was much less affected. Miliary abscesses had previously been observed by Kolesnikoff.

Fitz found the most extreme alteration in the part corresponding with the calamus scriptorius. The appearance most frequently met with was an infiltration of the adventitia of the veins with small round cells. Extravasation of blood was found in the perivascular spaces. The "miliary abscesses" were also seen, and in two instances actual abscesses were found (Fig. 75). So far as other organs were concerned, Fitz found numerous slight hemorrhages in the septum of the heart: no abnormal appearances were observed in the pharynx and in its submaxillary glands; the

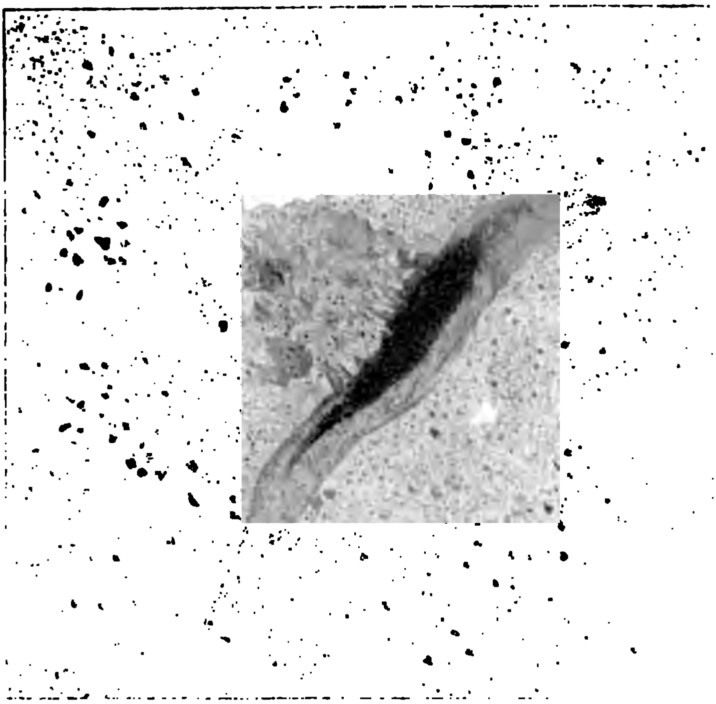

FIG. 75.—Extravasation or "Miliary Abscess" in the Cervical Cord in a case of Hydrophobia.

œsophagus from the bifurcation of the trachea downward was extensively œdematous.

In one case examined by Wickham Legg the kidneys showed cloudy swelling, but, as a rule, no pathological changes of importance appear to have been discovered in the thoracic and abdominal viscera. Hyaloid masses have been found in the medulla by several observers, but as these are met with also in normal specimens, it is not certain whether in these cases they were of any pathological significance.

Although in the microscopical appearances above mentioned there is nothing that can be regarded as specific of the disease, still Gowers is of the opinion that "the distribution of the lesions, their intensity in the lower part of the medulla and in the neighborhood of certain nerve-nuclei are, as far as I am aware, peculiar to the disease and constitute a distinguishing anatomical character."

Vesicles on the inferior surface of the tongue, once thought to be characteristic of the disease, are rarely found, and no special importance is now attached to them. The nerves of the part in which the bite is situated have been observed to present pathological changes: the myelin is found in a diffluent condition, the structure is softened, and the axis-cylinder is at times absent in many of the nerves. The same observation is recorded in the nerves arising from the medulla, such as the glosso-pharyngeal and the hypoglossal (Blodgett). Occasionally there is some hyperæmia about the region of the cicatrix, but in most cases no special change is observed.

The writer has already intimated that *treatment* of the disease is futile. Powerful drugs of various kinds have been used, but no authentic cases of cure have ever been reported. It was claimed at one time that curare had cured a case, but, although Shattuck and Curtis report a most systematic course of treatment with this drug in two cases, no favorable effects were observed; and this has been the experience of others who have tried the drug. Until something in the nature of an antitoxine has been discovered, it is hardly worth while to discuss the therapeutics of the already-established disease.

The *prophylactic treatment* so wonderfully carried out by Pasteur merits, however, the most careful scrutiny. Pasteur's attention was first called to hydrophobia in 1880, having visited a case in one of the hospitals under the care of Lannelongue.

In Pasteur's earlier experiments on animals he found that the virus existed not only in the saliva, but also in the brain, and that the period of incubation could be shortened greatly by inoculating the trephined brain of a healthy animal with the cerebral matter of a mad dog. Symptoms appeared in one or two weeks: by other routes the inoculation may not be followed by symptoms for one or two months. In fact, he soon found that the principal seat of the virus was in the central nervous system, where it may be obtained in great quantity and in a state of perfect purity. Virus obtained from this locality was therefore far preferable to the saliva, which contained quantities of micro-organisms. He later found that the virus existed in the whole nervous system of animals and in the salivary glands.

Pasteur next discovered that a given virus had its virulence modified by passing it through different species of animals. Inoculation from monkey to monkey attenuates the virus. Conversely, the strength of the virus is increased by passage through rabbits: the period of incubation is also shortened, so that by the time the one hundred and twenty-fifth passage had been reached this period is reduced to seven days. The spinal cords are virulent throughout their entire substance, and there is obtained by this method a virus of sufficient strength and reliability to be used for purposes of inoculation. By cutting up the spinal cord into fragments a few centimetres long and suspending them in a dry atmosphere their virulence gradually diminishes until it is lost, so that there can thus be obtained virus of any desired strength.

If a dog is to be made refractory to the poison of rabies, it is first inoculated with a cord so old that the virus is very feeble. The strength of the inoculation is gradually increased from day to day, each virus preparing the animal for the succeeding stronger dose until cords are used which have been drying only one or two days. The dog has now been successfully inoculated with very strong virus, and, feeling no bad effects from it, has become refractory to the ordinary "street rabies."

The brains and cords of rabbits used for these inoculations are prepared as follows: Having been removed from their bony casing, they are laid upon a plate with the basal surface upward. The parts which are necessarily handled should first be wrapped in paper. All instruments and utensils used are carefully sterilized by heat. The cords are dried by suspending them in bottles with a hole near the bottom for the purpose of ventilation; the two apertures are closed with cotton-wool plugs, and caustic potash is kept in the bottom of the flask to secure a dry atmosphere. On drying, the cords become crumpled and brittle and darker in color. The cord is used in preference to the medulla, as being more convenient to handle. The virulence is the same in both. The emulsion is prepared by beating up fragments of the cord about the size of a pea with sterilized veal-broth or with water in a half-ounce conical glass, which is afterward covered with filter-paper. The nerve-tissue is triturated by means of a glass rod, and the broth is added until a thick, turbid liquid amounting to about half a tablespoonful is produced. The broth used for this purpose is kept in a pipette bottle.

The inoculation experiments upon animals are carried out by trephining and inserting a drop or two of the emulsion beneath the dura mater. In this way absolute certainty of result is obtained as well as an exact period of incubation.

It was in July, 1885, that Pasteur first applied his protective inoculation in man. He had at that time rendered fifty dogs refractory without a single failure. A hypodermic syringeful of the emulsion is injected into the subcutaneous tissue of the region of the hypochondrium, as the tissue is here loose and is more rapidly absorbent than elsewhere. The patients are first inoculated with a cord fourteen days old, and the inoculation is repeated daily for nine days, each time with a cord one day fresher. In winter the oldest cords used are five days old, and in summer cords which have been drying for four days are also employed. The preceding is the ordinary treatment. The so-called "intensive treatment" is used for patients who have been bitten on the hands or on the bare feet, or for patients who have been bitten so long beforehand that it is necessary to complete the course of treatment more rapidly.

The *intensive method* consists in the omission of certain cords—for example, the weakest—and of some of the intermediary cords, and in the administration of the inoculations at shorter intervals than once in the twenty-four hours. If the first dose is given at 8 A. M. from a cord ten days old, the second dose would be given at 2 P. M. from a cord eight days old; the third at 8 P. M. from a cord six days old; and the fourth at 2 A. M. from a cord four days old. This series may be repeated at the same intervals, or, if the case be desperate—that is, if the patient has been bitten so long before treatment that the average period of incubation has already elapsed—the inoculation is carried even further, and the virus of only one day's drying may be used in the first twenty-four hours. By this intensive method it is claimed that better results are obtained than by the older, apparently safer, but slower, method.

The *first case* upon which this method was tried was Joseph Meister, a child nine years of age. He had been severely bitten on the hands, the legs, and the thighs, and when rescued from the dog was covered with blood and saliva. The animal was undoubtedly mad. Sixty hours after the accident (July 6th) the boy was inoculated in the right hypochondrium with half a syringeful of the emulsion of the cord of a rabbit which had died on June 21st. The cord had been kept fifteen days suspended in a bottle as above described. On the following day he was injected with a fourteen-days'-old cord, and so on daily or twice daily until, on July 16th, the thirteenth sitting, he was injected with a cord one day old. Healthy rabbits were inoculated with each preparation, and it was found that the older cords did not produce rabies, but the cords of July 11, 12, 14, 15, and 16 were all virulent, and the disease was therefore reproduced; Meister survived.

A child of ten, who had been bitten in the axilla and on the head, and who was not subjected to treatment until thirty-seven days after the accident, died of hydrophobia appearing eleven days after the end of the treatment. The question arising which of the viruses had killed the child, that of the mad dog or that prepared by Pasteur, her skull was trephined near the wound and a portion of cerebral matter was taken out and inoculated into rabbits, which died fifteen days later. Had the deaths of the rabbits been the result of the preventive inoculations, the incubation period would have been only seven days.

Of those who succumbed after treatment the majority were children who had been bitten in the face and who had only received the simple treatment, which Pasteur does not now consider sufficient for such cases. For those he now uses the intensive treatment, giving three or four inoculations daily, and reaching the one-day-old cord on the third day. Three courses are given during a period of ten days.

The difference in virulence of the cords is not considered by Pasteur to be due to a diminution of degree, but to a diminution in quantity of the virus contained in them. He is inclined to believe that the rabies virus is made up of two distinct substances—the one living and capable of multiplying in the nervous system; the other not living, but capable, when present in suitable proportions, of arresting the development of the former. In other words, he believes in a "vaccinal" matter associated with the microbe, the latter dying more rapidly in the dried cords than the former.

Vaccine inoculation for protection from small-pox is sufficient if performed three days after exposure, as the period of incubation of the vaccine is only nine days, while that of small-pox is twelve days. So with the vaccine of rabies: it must be given sufficient time in order to do its work more effectively.

The *death-rate*, according to French statistics, amounts to 30 per cent. after efficient and early cauterization. When these precautions are not used it rises to 80 per cent. According to Gowers, when no preventive measures are adopted at least half, perhaps two-thirds, of persons bitten escape. A moderate estimate of the death of all persons bitten by rabid animals except wolves is probably 20 per cent., whether the bites have been cauterized or not. The death-rate from wolf-bites is as high as 65 per cent., and when the face and head are bitten it reaches 88 per cent. Indeed, in Russia it is believed that every person bitten by a mad wolf dies. The incubation period following the bite of this animal is quite short, owing to the number and the nature of the bites. It is not probable that there is any difference in the viruses of a mad dog and a mad wolf.

The results obtained by the work as carried on in Paris at the

Pasteur Institute since the beginning of the employment of this method are summarized and discussed very carefully and fairly in the *Annales de l'Institut Pasteur.* All cases are placed in one of three categories: Class A consists of those bitten by animals shown to have been rabid by experimental inoculation; Class B consists of those bitten by animals declared to be rabid by veterinary authority; Class C includes those bitten by animals supposed to have been rabid. The following table gives the figures of these different classes for 1893:

Bites of Head.			Bites of Hands.			Bites of Body and Legs.			Total.		
Patients.	Died.	Mortality, per cent.	Patients.	Died.	Mortality, per cent.	Patients.	Died.	Mortality, per cent.	Patients.	Died.	Mortality, per cent.
A, 12	0	0	80	0	0	40	0	0	132	0	0
B, 89	0	0	534	3	0.56	385	0	0	1008	3	0.30
C, 34	0	0	243	1	0.41	231	0	0	508	1	0.20
135, Total.	. .	. .	857, Total.	4	0.46	656, Total,	. .	. .	1648	4	0.24

The statistics for each year from the beginning up to the present time are given below:

Years.	Patients Treated.	Died.	Mortality, per cent.
1886	2,671	25	0.94
1887	1,770	14	0.79
1888	1,622	9	0.55
1889	1,830	7	0.38
1890	1,540	5	0.32
1891	1,559	4	0.25
1892	1,790	4	0.22
1893	1,648	4	0.24
Total	14,430	72	0.50

These figures apparently afford ample proof of the success of the Pasteur method.

Tizzoni has experimented with a protective substance produced by treating the cords of infected rabbits with peptones. An emulsion of the cords in peptones parts with its virulence entirely in twenty-four hours. The flocculent deposit obtained is preserved in glycerin. Tizzoni has been able not only to render rabbits immune, but also to check the symptoms of rabies after they had already developed. This method of treatment has not yet been applied to man. (See Appendix.)

XX. ACTINOMYCOSIS.

ACTINOMYCOSIS (ἀκτίς, ray, μύκης, fungus) is an affection characterized by the presence in the tissues of a vegetable parasite (actinomyces) which gives rise to a chronic inflammatory process. This disease is found both in animals and in man. In the former it gives rise to a granulation or sarcoma-like tumor, and it has been described, before its true nature was understood, under a variety of names, such as "big jaw," "swelled head," and "lumpy jaw." Many cases described as sarcoma in cattle were undoubtedly forms of this affection. In man the growth is accompanied by a suppuration, which is not due, however, to the organism, but to a mixed infection with pyogenic cocci.

Langenbeck was one of the first to notice the presence of the parasite in a case of vertebral caries. Lebert was, however, the first to publish, in 1848, a description of the same organism, which he found in an abscess of the thorax. He did not, however, recognize its significance. Robin observed similar bodies also in pus, and Rivolta in 1868 and Perroncito in 1875 found the organisms in the jaws of diseased cattle. The first scientific description of these organisms came from Bollinger, Israel, and Ponfick in 1877, 1878, and 1879, respectively. Since then a large number of cases have been observed and described in man. In America, Belfield first recognized the parasite in cattle, and Murphy reported the first case of actinomycosis hominis. According to the latter, up to January 1, 1891, there had been reported two hundred and fifty cases of the disease in man.

A description of the organism will be found on page 76. It may be briefly stated here that the organism is known as *actinomyces*, or the ray fungus, and it appears in pus or on granulations as minute granules varying in size from a grain of sand to a pin's head (Fig. 22). These granules, which are yellow in color, are easily seen by the naked eye. If pressed down with a cover-glass, they readily flatten out, while possibly a distinct gritty sensation is transmitted to the finger, owing to the presence of calcareous matter. With a low power of the microscope the fungus will be recognized scattered over the field in the form of irregular patches, which might at first be mistaken for granular débris, but which, by more exact examination with a higher power, will be observed to have the characteristic appearance. The rosettes of clubs mingled with pus-cells and fragments will then be found. By pressing upon the cover-glass the rosette is broken up and the club-shaped masses are seen separately. If the yellow granule is picked apart in water, the central portion of the fungus appears to be a structureless core.

Cultures of actinomyces are made with great difficulty. Agar-agar and egg-albumin, blood-serum, bouillon, and gelatin are the media used for the purpose. The growths taken from plates and grown in blood-serum develop at the end of four or five days. According to Babes, cultures obtained by him grew mostly in the depths of the culture medium and rarely on the surface. Attempts to transfer the actinomyces from one animal to another by mixing them with the animal's food have not succeeded, but inoculations have successfully been made by introducing the granules into the peritoneal cavity of rabbits; also by introducing the infective material beneath the skin, into the veins, and into the abdominal cavities of calves. The cow appears to be the most susceptible of all animals. Although the disease is found in cattle, yet in reported cases it does not appear that it has been transmitted to man in his food, and the disease has not been observed in carnivorous animals. The few observations that have been made, tending to show that the meat of animals is the source of disease in man, have not sufficed to demonstrate this satisfactorily. Hence it has not been the custom in many places to condemn the entire animal when a part only is affected. There are no observations which prove that it can be transmitted by milk. According to Boström, who carefully analyzed a series of cases, the disease appears to begin in the autumn, and the ears of grain in which the fungus probably grows are the carriers of the disease to man and to animals. In one of this author's cases the patient acknowledged that he was in the habit of chewing ears of barley or of rye, and in the much-quoted case of Soltmann the patient, a boy, swallowed an ear of barley, which caught in the œsophagus and could not be coughed up. Perforation occurred, and mycotic abscesses formed around the vertebral column and elsewhere. Johne found frequently in the tonsils of hogs ears of grain containing unmistakable growths of actinomyces. Jensen observed an outbreak of the disease in cattle due to feeding them with grain which had been taken from a soil reclaimed from the sea. It seems probable that the most frequent route of infection is the mouth and the pharynx, the organism becoming attached to and growing in some of the numerous inflammatory processes common to this region. The cavities of carious teeth and the follicles of the tonsils appear to be localities that afford a soil favorable to the growth and development of this organism, from which foci it is subsequently distributed throughout the system. After once having gained a foothold, the parasite is said to be conveyed to distant parts of the body through the blood-current and not through the lymphatics.

In man the disease presents two salient features—the formation of abscesses and the presence of yellow granules in the pus, and granulations of these abscesses. The swelling does not have a well-defined border, as seen in cattle, in which it resembles a tumor, but it is more or less flattened and disseminated, and is accompanied by the growth of an indurated connective tissue which is very characteristic. There is usually, later, a false fluctuation at certain points, due to the presence of the soft, fungous mass of granulation tissue. Presently the skin becomes a deep red and the abscess opens. The granulating surface has a yellowish or a violet color. Pressure brings a small quantity of thin sero-purulent or cheesy material. In some cases a few drops of thick pus will ooze out after lancing the abscess, and with them a number of striking sulphur-colored granules. On probing a sinus thus formed it will be found that the disease has involved the adjacent muscles, which are so infiltrated and matted together as to impede their movements. The nerves are also involved in the induration, and in later stages the bone becomes affected and in it cavities form. The jaw is usually the part most frequently attacked, and later the teeth drop out and the pus-cavity communicates with the mouth. In the mean time new fistulæ form and communicate with the original focus. The disease does not attack the interior of bone as in cattle, forming a spina ventosa, but rather confines itself to a multiple caries with the formation of osteophytes (Partsch).

If the inflamed mass is laid open at a post-mortem examination, the sinuses are found to resemble those seen in connection with tuberculosis of bone. There is a lining pyogenic membrane composed of fungous granulation tissue of a yellowish or a reddish-gray color, which tissue is readily scraped away. A central pus-cavity is rarely found. A number of minute abscesses, however, are seen in the walls of the inflamed mass. Other abscesses may be found in the immediate neighborhood, either entirely independent of the original focus or communicating with it by fistulous tracts. The yellow grains are to be found in the secretions of all these various cavities and also in the walls.

A cross-section of the abscess-wall shows it to consist of a sarcoma-like tissue. It has been said to resemble so closely round-cell sarcoma as to be almost indistinguishable from it were the yellow grains absent. In other places spindle, epithelioid, and giant-cells are seen. In the peripheral portions of the disease the abscess-wall consists of a dense fibrous tissue surrounding a cluster of cells, in the centre of which is the actinomyces (Babes).

When once the parasites begin to develop in the tissues a growth of sarcomatous connective tissue is built up around them, forming a barrier which probably tends to retard their growth. The cells nearest the centre of this nodule undergo fatty degeneration, and break up and leave a more or less fluid substance in their place, and in this way a miliary abscess is formed. Large abscesses form by fusion of several smaller ones.

The progress of the disease is slow, as the inflammation is of a chronic type. Infection takes place most frequently through the mouth and the pharynx, but the organism may find an entrance to the system through the air-passages or through the skin. In any case a wound, however small, is necessary for inoculation to take place.

When *infection takes place by the mouth* in the less severe forms of the disease, the patient comes with a history of toothache, with swelling at the angle of the jaw, and with difficulty of swallowing and of opening the jaw. The external tumor reddens and softens, and fluctuation is followed by an opening and discharge of pus containing the characteristic yellow granules. After some temporary improvement the swelling continues to spread and the abscess opens into the cavity of the mouth. Many cases can be arrested at this point by a radical operation which removes the entire diseased mass. A very characteristic symptom, according to Partsch, is the rigidity of the jaw caused by the induration of the surrounding muscles.

If the affection is allowed to continue untreated, however, the bone of the lower jaw becomes involved, the teeth drop out, and several of the adjacent muscles are destroyed. As the disease works its way downward it follows the line of the sterno-mastoid muscle to the clavicle, involving on its way nearly all the structures of the neck, including the vessels. The pus, which burrows about inside the diseased mass, finds its way to the surface at various points in the neck, and even into the œsophagus, so that food may be discharged through the fistulæ. A muco-purulent expectoration from the lungs shows that the disease has reached these organs, and on its way it may have destroyed the clavicle. If portions of the fungus find their way during this process into the circulation, the heart may become involved in the disease, and small tumors may form in the substance of its walls and in the pericardium. Metastatic deposits may be found in the spleen, the liver, the brain, and the kidneys.

When the upper jaw is the seat of the disease the prognosis seems to be still more unfavorable. Here the cheek is involved in the inflammatory process, and abscesses may form and break as high up as the lower eyelid, which probably will be very much swollen and œdematous. Here also the disease appears to begin in a carious tooth. With the discharge of pus there may be symptoms of nasal catarrh, showing that the disease is spreading in the direction of the nose. The swelling soon involves the whole cheek, and then spreads backward to the region of the ear and the temple. The jaws are often difficult to open at this stage, and the fetor of the breath may be well marked. If an inspection of the throat can be made, the tonsil and the fauces are often found swollen and red; the gums are also swollen, and many of the teeth are loose. These changes follow one another slowly, and there are periods when the disease, after surgical treatment, appears to be improving; but although, superficially, there is a diminution in the severity of the symptoms, there is a gradual spread of the infection in the deeper parts, where nothing seems to be allowed to stand in the way of the progress of the disease. In working upward it may penetrate the base of the skull and the membranes, and even invade the brain itself. From the pharynx or œsophagus it may reach the posterior mediastinum, and so affect the bones of the spine that they appear to have undergone an extensive caries. Abscesses forming in this locality may perforate the intercostal spaces and may break externally in the dorsal region. In rare cases the disease may begin with an infection of the tongue: Hochenegg reports such a case. The patient was a young man who looked after cattle and who was in the habit of chewing ears of grain. On one occasion he thought he had wounded his tongue with the edge of a carious tooth. Two months later there was a swelling in the right half of the tongue about the size of a cherry. This swelling was excised with a wedged-shaped piece of the tongue, and the patient was cured.

Infection through the respiratory tract is supposed to be due to the inhalation of colonies already forming in the mouth or the throat. A case is reported in which a tooth was inhaled into the lung and became the starting-point of the disease in that organ. The direct infection of the lung by inhalation is doubted by many, but cases are reported in which it is probable that the fungus or its spores were inhaled directly into the lung with the inspired air. The left lung is said to be more often affected than the right. The first symptom of the disease may be a pain in the side ushering in an attack of pleurisy. In a case reported by Boström there appeared soon after the pain a redness and swelling at the level of the eighth rib. On making an attempt to excise this swelling the tissue was found to be almost of sole-leather hardness, but pus eventually was reached. This inflammatory induration gradually spread up and down, so that six months later, when the patient died, it had invaded the thorax-wall and had worked its way through the diaphragm into the liver and along the spinal column to the pelvis. The expectorations in this case were peculiar, and were regarded by Boström as pathognomonic of the disease. On washing the muco-purulent sputa in water they were found to be branched in a way that showed them to be casts of the finer bronchi, and to contain the actinomyces granules. This author observed the same condition of the sputa in another case.

The effect upon the lung parenchyma is to produce a proliferation of round cells which undergo fatty degeneration. Patches of pneumonia and peribronchitis are thus formed, or, if the infection is near the surface of the lung, pleurisy may develop. Abscesses eventually form which break into the bronchi. The apices of the lungs are usually unaffected. There is considerable resemblance in the clinical course of the disease to chronic or fibroid phthisis. At the autopsy the tissues about the diseased part are found to be exceedingly dense, beneath which are found abscesses opening into the pleura or into a pulmonary cavity. It would be difficult, says Babes, to distinguish the disease from tuberculosis of the lungs were it not for the presence of the yellow granules. There is often great contraction of the thorax when the disease has existed for some time in that cavity.

Intestinal actinomycosis is due to the swallowing of the organism with the food. Colonies are said to form upon the epithelium of the intestinal wall, and there follows infiltration of the deeper layers. The mucous membrane may in this way become covered with white patches, and in such cases small nodules, about the size of a pea, may be found in the submucous tissues. In the mucous membrane these nodules soften and form ulcers which may eventually perforate into the peritoneal cavity. In a case reported by Boström such a complication resulted in the formation of two abscesses—one in each iliac fossa—that broke and discharged externally. At the autopsy it was found that the left abscess had involved the ovary. Murphy reports a case of a large abscess in which the spleen was floating, and which probably was caused by actinomyces. Several cases are mentioned in which the processus vermiformis has been found attached to or opening into an actinomycotic abscess. The fungus may be found, in cases of intestinal actinomycosis, in the evacuations. The symptoms of the intestinal form of the disease are those of acute catarrh following a digestive disturbance with diarrhœa in recurring attacks. The complications are those of chronic localized peritonitis.

Invasion through the skin occurs occasionally. A number of cases are reported of inoculation through trivial wounds and also after surgical operations. Partsch describes a case of the development of the disease in the cicatrix which formed after an amputation of the breast. Hochenegg records a case of a girl who slept in a stable with cattle, and who apparently inoculated a suppurating wen of the cheek with the parasite. The same author reports an actinomycotic abscess of the abdominal walls due to the blow of a hammer. Many cases are reported in which the source of the infection could not be detected. A striking example is the primary actinomycosis of the brain reported by Bollinger.

The *prognosis* of the disease when it is situated superficially is not unfavorable. If the mass is promptly removed the danger of return is not great, and a large number of cures have been reported. When internal organs become involved the disease is almost certain to terminate fatally. It is essentially a chronic disease, and the patient may live from one to three years.

The *treatment* of actinomycosis consists in an attempt to remove as completely as possible the entire mass of affected tissue. In the small primary nodules about the neck and the face this removal may satisfactorily be accomplished. If the disease has progressed any distance downward into the neck, a free incision should be made along the line of the sterno-mastoid from the ear to the clavicle, and all the tissues should carefully be dissected out. The operation should be as thorough, if possible, as that for cancer. Decayed teeth should be removed; the bone of the jaw should be cut away or be so laid open as to make it possible to scrape away all evidences of diseased tissue. When it is impossible to excise the mass and leave a clean wound, all sinuses should be laid open and followed relentlessly to the end, and their walls should be scraped thoroughly with the curette. The exposed surface should then be washed with a solution of corrosive sublimate. Solutions of nitrate of silver, which are supposed to exert a poisonous influence upon the fungus, may be injected into suspected nodules in a strength of 1:1500 or be applied to the granulating surface of a wound. Internal medication appears to exert no influence whatever upon the growth of the parasite.

In a case recently operated upon by Mixter, the first reported case in man in Boston, the disease was found to be situated in the neighborhood of the umbilicus. The patient was a city laborer, fifty-six years of age. He first noticed, three months before, a lump in the abdominal wall that had grown slightly at the time of the operation. There was on examination an indurated mass surrounding the umbilicus about the size of a Mandarin orange. At the operation the peritoneal cavity was opened, and the growth was found adherent to the omentum and intestine. In the interior of the mass removed were found cavities containing a thin whitish fluid. On laying open the growth freely, two fish-bones, the size of knitting-needles in thickness, were found. The pus contained opaque white granules which proved to be actinomyces. The patient made a good recovery.

The *disease in cattle* has much less tendency to cause suppuration. In Europe the disease is prevalent in river-valleys and in marshes and on land reclaimed from the sea, and it appears to occur more frequently in the young than in the old and more often in winter than in summer. It appears in the form of tumor-like masses without indications of an inflammatory process, and many of the cases of "osteo-sarcoma" of the jaw in animals reported in former times were undoubtedly cases of actinomycosis. The tongue is often affected in animals, and the infiltration of this organ is accompanied by the subsequent induration often seen in this disease, but which in this case is more marked than elsewhere. The condition known as "scirrhous tongue" (or *Holzzunge*, wooden tongue) is thus produced. This disease of cattle is not limited to Europe, but it has been found quite extensively in cattle in the United States, particularly in the West.

XXI. ANTHRAX.

THE nomenclature of this disease is somewhat confusing. It is known in England as "splenic fever," and in Germany as *Milzbrand*. In France the term "anthrax" is applied to another affection (carbuncle), and "charbon" is substituted. In man the disease is known as "malignant pustule" in all countries. Anthrax prevails in various portions of Europe, particularly Russia, Hungary, France, and Saxony. It is known to exist also in Siberia and in India. Anthrax does not prevail in the United States, but isolated examples of it are occasionally seen in man. It appears at times as an extensive and fatal epidemic. Thus, according to Gronin, there perished from this disease in Novgorod, Russia, alone during four years (1867–70) more than 56,000 cattle and 528 men. The greatest losses are incurred during the summer season. The domestic animals most susceptible are cows, sheep, and horses, the ass, the goat, and swine being less often attacked. Mice, rabbits, and guinea-pigs are also particularly susceptible, and consequently are used in laboratory experiments. Anthrax can be communicated only with difficulty to dogs and poultry. The epidemics in animals occur most frequently in swampy regions where decomposing vegetable material abounds. Saline elements in the soil, combined with warmth and moisture, seem to favor the development of the virus. The disease consequently is found along the borders of rivers and in malarial districts.

The organism which Davaine demonstrated to be the cause of anthrax is known as the "bacillus anthracis." Owing to its size it was easily seen with comparatively low microscopic powers in the blood, and was therefore the first of the pathogenic bacteria to obtain recognition. A description of the organism is given on page 70.

One of the most striking peculiarities of this organism (Fig. 20) is the formation, when in contact with the air, of spores which have remarkable powers of resistance to the external agencies that ordinarily destroy bacteria. These spores do not form in the body of the diseased animal, the bacillus here reproducing itself solely by division. The organisms are released from the body in the bloody discharges of the animal. It is probable that the milk of diseased animals does not contain bacilli, but, as contamination is easy by mixture with blood or with dirt, such milk should not be used.

After the death of the animal the liberated bacilli elongate and spores are formed. The bacilli are easily destroyed, remaining alive but a few days. Fluids containing bacilli can retain their infective properties only a few days, unless spores are produced. These spores are called "durable spores," owing to their great vitality, and they eventually, under favorable conditions, grow to rods and long threads: this is the complete cycle of their development. The spores are found in surface soil, or, according to Pasteur, in deeper soil when the animal is buried, and subsequently they are brought to the surface by earth-worms. Koch, however, does not accept the earth-worm theory. According to him, the spores cannot develop at any great depth, as they need a temperature of over 18° C., and at the depth of ground at which the animals are usually buried the temperature rarely rises above this point.

Karlinski examined the carcass of a sheep dead of anthrax that had been dug up by wolves. He found on it a number of snails. Thinking that snails might spread the virus, he made a series of examinations which showed that the snails were insusceptible to the virus, that the bacilli passed through the intestinal canal without diminution of their vitality, and that they remained eleven days in a healthy condition in the intestine.

Koch has shown that infusions of hay are not favorable for the development of the bacilli, owing to the acidity of the solution. The addition of an alkali so neutralizes this condition that growth takes place. In localities where epidemics suddenly break out there is probably an alkaline soil and a dead vegetation. After a damp season with an overflow of the banks of a river a favorable culture-fluid is formed, and the growth of the bacilli from the spores, which have up to this time been blowing about as dust, begins to take place. When once the spores have developed the disease is with difficulty exterminated from a neighborhood.

The organism obtains an entrance into the body in one of three ways—namely, by inoculation through wounds of the skin, by inspiration through the air-passages, and with food through the intestinal mucous membrane. In infected districts the dust of the air is filled with the organisms, and this dust is grimed into the hair and the hide, whence the bacteria can readily be rubbed into any abrasions on the surface of the body. It has been supposed that the virus when taken with the food found its way into the system solely through wounds of the mucous membrane. It has, however, been demonstrated that the spores develop readily in the upper portion of the intestine of sheep, but not in the lower portion. The bacilli are destroyed by the gastric juice, while the spores pass unharmed through the stomach. Food containing spores was given by Koch to sheep, with the result that all succumbed to the disease, whereas portions of the spleen of a diseased guinea-pig, containing only bacilli, did not affect them. It is probable, therefore, that the organism can penetrate the healthy mucous membrane.

Koch also demonstrated the possibility of infection through the respiratory organs. A mouse placed under a bell-glass, where dust containing bacilli had been deposited, succumbed to the disease.

Malignant pustule is the name of the disease as it is found in man. It is known also as "wool-sorter's disease," but this designation is said by some authors to be given to that variety which is unaccompanied with an external primary lesion.

Infection occurs by direct inoculation into either a scratch, an abrasion, or a small wound of the skin in the great majority of cases. Individuals who come in contact with the diseased animals or with their hides, and operatives who are at work in factories where goods made from the hair or the hides of these animals are manufactured, are most liable to contract the disease. In the neighborhood of Boston the disease has been observed among operatives in curled-hair factories and among the longshore-men who handle the hides imported from infected districts. The hands in this way come in contact with the spores, and inoculation takes place later by scratching the skin. The virus may also be conveyed by flies. Infection by the consumption of diseased meat is possible, but it rarely happens, as the mucous membrane of man is insusceptible.

Contagion from man to man is also very rare. Korányi mentions a case of a woman who, while afflicted with the disease, visited her daughter at a place where no case of anthrax had been known for thirty years. After the departure of the mother the daughter developed symptoms of the disease and died. Korányi had never seen a case of inoculation direct from surface to surface, as in syphilis.

The period of incubation lasts from one to three days. The most frequent seat of the primary lesion is the face. The first noticeable symptom is a sensation of itching, which accompanies the appearance of a small red spot or papule resembling closely a flea-bite; twelve or fifteen hours later there forms a small vesicle, which is not distended, and which contains a brownish or a bluish fluid. If the vesicle is not scratched, it gradually dries up and forms a scab. The surrounding skin is somewhat reddened, indurated, and swollen. This change is the precursor of the gangrene which follows. The affected area enlarges in depth and width, the color darkens, and finally there is formed a black eschar, which, at first superficial, gradually involves the deeper layers of the skin. This black spot varies somewhat in size from 2 mm. to 2 cm.; on the surface it is hard and dry, and there is no indication of suppuration. The slight burning sensation which existed during the formation of the vesicle now disappears, and the lesion is characterized by an entire absence of pain. Presently a circle of new vesicles forms around the eschar, giving to it the appearance of the seal of a ring set in pearls (Bourgeois). In some cases it looks not unlike a vaccine vesicle. The vesicles run together, and the fluid within them is more or less discolored by the presence of blood-corpuscles. In the mean time the surrounding skin may become reddened, although it does not always change color. There is considerable swelling in the immediate neighborhood, so that there forms a circular tumor distinctly raised above the level of the surrounding skin. It becomes later more or less reddened and indurated, and the so-called "carbuncular tumor" is thus formed. If the disease continues to progress, the surrounding parts become affected, and an œdematous swelling makes its appearance, which may in some cases be very extensive. In a case of malignant pustule of the neck in a robust young man under the writer's care the whole side and front of the neck became so swollen that preparations for tracheotomy were made in case dyspnœa should develop. The tumor, however, subsided and the patient made a good recovery.

If the œdema continues, fresh crops of vesicles often appear, and the skin becomes more or less affected and the adjacent lymphatic glands are enlarged. The development of these local symptoms occupies from three to nine days. Finally, a line of demarcation forms around the eschar and the slough separates, leaving a granulating surface, or cicatrization may take place under the scab without any suppuration. According to Raimbert, the striking peculiarities of the malignant pustule are the absence of pus or sanies in the initial lesion, the absence of pain, and the existence of a vesicular areola, not purulent and of limited dimensions.

In less favorable cases the inflammation of the surrounding tissues is more marked and it assumes an erysipelatous appearance. Bullæ form which are filled with bloody fluid, and the parts below are ecchymosed. Suppuration and gangrene finally supervene. Malignant pustule is found almost always on exposed surfaces of the body, such as the face, neck, hands, and shoulders. It is very rarely found elsewhere.

In rare cases the eschar may be wanting, and an œdematous swelling is then the only symptom of the local condition. In such cases it has been suggested that an internal infection has taken place. This swelling may sometimes be very extensive. The lips, the eye, the eyelids, the tongue, the chest, and the upper extremities may become involved in this œdema. The swelling is soft and diffuse, and is without change in the color of the skin. It is accompanied by grave constitutional disturbance.

For a day or two after the beginning of the disease there may be no marked disturbance of the general health, and the patient may even continue at his work. In some mild forms of pustule there may be no fever. At the end of a few days the patient begins to complain of malaise, nausea, pain in the muscles, and headache, which symptoms are accompanied with a rise of temperature. In severe cases the heart's action is weak and rapid, and there is an oppressive anxiety, with rapidity of the respiration. There is slight icterus and other symptoms of septicæmia. The prostration is very great, and in the last stages of the disease the condition of the patient is like that of one in the algid stage of cholera.

In some cases tetanic convulsions and trismus precede coma. When infection takes place through the intestinal canal, the disease begins with debility, depression of spirits, and malaise, and probably a chill. In addition to these symptoms of constitutional disturbance there are symptoms pointing toward the intestines as the disease develops. Hemorrhages may occur from the mouth and the nose, and vomiting is followed by a bloody diarrhœa. Difficulty of breathing and cyanosis, with great restlessness, are also seen in this form. An eruption of small phlegmonous or carbuncular inflammations often occurs on the skin. The diagnosis in such cases is often extremely difficult, particularly in isolated cases occurring independently of an epidemic. Microscopic examination of the blood or an inoculation of an animal furnishes the only conclusive evidence of the disease.

The *pathological appearances* are well shown in an examination of a section taken from a fresh pustule of three days' duration.

An eschar is seen situated beneath the epidermic crust and the rete mucosum, involving the upper layers of the cutis vera and surrounded at its lower border by a round-cell infiltration. A few anthrax bacilli are found in the superficial scab and in the rete. In the eschar the bacilli are very numerous; the papillæ are distended and filled with them, but they were not found in the hair-follicles, the sebaceous glands, or the blood-vessels. The periphery of the eschar is occupied by micrococci and other forms of bacteria (Straus). At a later stage of development the eschar involves the whole thickness of the cutis. The bacilli may be found in and near the eschar in some cases for eight or ten days, but not always, for the putrefactive bacteria which are found surrounding the eschar appear to have destroyed the anthrax bacilli.

In two very acute cases reported by Cornil and Babes a post-mortem examination failed to show the bacilli in the neighborhood of the pustule or in the adjacent tissues. There were no bacilli in the blood of the heart nor in the blood of the cutaneous vessels, but sections taken from the different organs gave positive results. The bacilli were found in the fibrous tissues which accompanied the vessels of the lungs and in the subpleural connective tissues. A section of the mucous membrane of the stomach showed the bacilli crowding the mucous follicles, while but few organisms were found in the blood-vessels.

Rosenblath reported a case of a boy eight years of age who died of malignant pustule on the seventh day. An examination of the blood and the organs showed the existence of only a moderate number of bacilli, and those apparently not in an active state of development. The number of cocci found in the blood and in the fluid of the peritoneal cavity was very great.

In intestinal anthrax an examination of the mucous membrane showed, in a case reported by Cornil and Babes, œdema and ecchymosis in the jejunum, as well as ulcers. The mesenteric glands were enlarged. The bacilli were found in the blood-vessels, in the tissue comprising the bases of the ulcers, and in the mesenteric glands. In the Dupuytren Museum there is a specimen of a stomach, taken by Verneuil from an individual who died of anthrax, containing gangrenous patches and inflammation of the intestine.

Decomposition of the cadaver begins rapidly. The blood is thick, tarry, and shows no tendency to coagulate. There is a tendency to hemorrhages in the serous and mucous membranes. The spleen is often enlarged and ruptured, but not invariably.

The *prognosis* of anthrax in man varies greatly. In general man may be said to be an insusceptible animal; consequently in most cases seen in young and healthy individuals in America the disease runs a mild course. When the pustule tends to remain localized and is uninflamed, the general disturbance of the system is caused by the toxic products of the organism, but when once a general infection of the system takes place the disease in all probability will terminate fatally.

Although occasionally some of the mild cases of malignant pustule recover without treatment, it would be unsafe to allow any case to pursue its course without interference. The *treatment* should be radical, and it should aim to remove the infected area as thoroughly and promptly as possible while it is still localized. One of the most effective methods of effecting this removal is excision. The knife should be carried well outside the areola surrounding the eschar. The wound should then be washed or mopped with a solution of corrosive sublimate (1 : 1000), and an antiseptic dressing, or, better, an antiseptic poultice, should be applied to the wound. The character of the dressing will be determined by the nature of the wound. The best substitute for the knife is the actual cautery, which should be applied deeply around and beneath the edges of the eschar. Small pustules may be treated by the application of liquefied crystals of carbolic acid. A small incision would favor the deep application of the acid. Larger pustules may be incised freely, and be dusted with powdered corrosive sublimate, which favors the destruction of the entire mass (Whittaker).

Cutaneous injections of carbolic acid (from 5 to 10 per cent. solution) around the edges of the eschar may arrest the progress of the disease, but this form of treatment is less thorough than those already mentioned. The employment of toxines may eventually be made successfully in the treatment of this disease. Ogata's experiments are suggestive in this connection. This author states that he succeeded in eliminating immunizing substances from the blood of animals insusceptible to anthrax. This substance he describes as a ferment which, when injected into animals, acts as a curative and a protective agent. The bacillus pyocyaneus has been found to exert an inhibitory influence upon the development of the anthrax poison, and it is possible that this organism may in consequence eventually be employed as a therapeutic agent. Internal medication is probably useless when once general infection is established, but a liberal and judicious use of alcoholic stimulation may enable the system to battle successfully against the generalization of the disease.

Anthrax in Animals.—The disease may develop in animals either with or without local manifestations. The latter form occurs more frequently in sheep and cows. It comes on sometimes with great violence, and it is then known as the "apoplectic" form. A healthy and robust animal may be taken suddenly with convulsions, foaming at the mouth and nose, and may die in a few minutes, or it may rally for a time and the attack again begin. The breathing is increased in rapidity and is irregular, and the heart's action becomes weak and rapid. Symptoms of anæmia of the brain show themselves. There is dilatation of the pupils, trembling, convulsions, foaming at the mouth and nose, and bloody evacuations of bowels, and in a few hours the animal is dead (Korânyi). The disease may, however, last longer, in which case there is a chill with high fever, swelling of the eyelids and the nasal mucous membrane, and attacks of colic. This is the true splenic fever.

Anthrax may develop in animals with a carbuncular swelling or swellings, which are often seen in horses. They appear as circumscribed swellings (hot and tender), which, as they grow, become softer, cooler, and less sensitive. If they are deeply situated, the skin is not discolored and there is a good deal of surrounding œdema. In the skin the carbuncle is reddened or dark-colored. Occasionally the local swelling assumes an erysipelatous character, and emphysematous gangrene eventually develops. The carbuncular swellings are seen on the head, the neck, the belly, and the extremities.

A post-mortem examination shows the blood to be thick, tar-like, and incoagulable. The vessels of the subcutaneous tissue, the mucous membranes, the alimentary canal, and the mesenteric glands are distended with blood, and there are numerous blood-extravasations which seem to break up the muscular tissues and the parenchyma of organs. The spleen is enormously enlarged. Its parenchyma is softened to a semifluid mass of a violet or almost black color. The capsule at times is ruptured, and the contents escape into the peritoneal cavity. The mortality of this disease in animals is placed at 70 per cent., and by some authors as high as 75 to 80 per cent.

The thorough study that has been given to the organism which is the cause of this disease should leave the sanitary authorities no excuse for not adopting the most scientific means of disinfection for infected districts, for on no other basis can there be any hope of stamping out the disease when it has once established itself.

XXII. GLANDERS.

GLANDERS is an infectious disease, characterized by the formation of nodules and ulcers in the mucous membranes, principally of the nares, and in the skin. It is found in the horse and other domestic animals and in man, and it is caused by a specific pathogenic organism. The term *farcy* (*farcio*, to stuff) is applied to that variety which involves the lymphatics and is seen principally in the skin. *Equinia* is a name which has been employed also to a limited extent to designate this disease. Its Latin name is *malleus.*[1] The French call it *morve*, and the Germans *Rotz* and *Wurm*.

Glanders is found not only in the horse, but also in asses and mules, sheep, goats, and rabbits; mice and guinea-pigs are susceptible to the disease when inoculated, but mice are not suitable for inoculation-tests, as they are apt to die of septicæmia. Dogs are but slightly susceptible. Glanders appears to occur among horses in all climates and in all countries.

According to Virchow, this disease should be classed with tubercle and syphilis under the general head of granulomata: in many respects it resembles these diseases closely, and has often been mistaken for them. The granulation-like tumors which are so characteristic are caused by the presence in the tissues of the bacillus mallei. This organism was first described in 1882 by Löffler and Schütz, but the organism was also discovered simultaneously by Babes and Israel. A description of this bacillus will be found on page 62 (Fig. 18). Though always due to the same organism, glanders manifests itself in many ways in different individuals, so that in an epidemic in one stable dissimilar types of the disease are seen in different cases. There may be infection of the lymphatic glands or of the nasal mucous membrane, or an inflammation of the lung or metastatic abscesses, with general febrile disturbance. The attempt formerly made to separate the disease into several

[1] A name given by the ancient Latin writers on veterinary medicine to various diseases of the horse. The original meaning is *hammer*: the connection is obscure—perhaps from the painful and fatal character of such diseases, or from *malleus*, meaning the mallet of the butcher at a sacrifice; also (in the diminutive form *malleolus*) a fire-dart. The alleged Greek word *μαλίς* or *μαλία* is probably a corruption of the Latin.

varieties should therefore be abandoned. Experiments show that the bacilli gain an entrance into the body through slight wounds, and that inoculation takes place through scratches and abrasions of the mucous membrane of the mouth and the digestive tract. Fränkel adopts the view that horses acquire glanders by inhalation, but the nasal symptoms which are so prominent a feature of the disease are attributed by Baumgarten to the general systemic infection which has previously taken place. The disease can be transmitted from mother to fœtus *in utero.*

Babes and Nocard succeeded in obtaining an infection of guinea-pigs through the intact skin, but it is probable that the disease, clinically, is not propagated in this way. It is more probable that infection takes place through the intact mucous membrane, and it appears that infection probably does take place in the horse frequently through the air-passages by the inhalation of the dried organisms in the form of dust. In this way glanders may be communicated from one animal to another. It is said that glanders has been transmitted to menagerie animals by feeding them with the flesh of diseased horses. Decroix, however, disproved this theory by eating with impunity the meat of a glandered horse, both cooked and raw.

In man the usual mode of infection is through some slight wound of the hands that is inoculated while grooming or feeding diseased horses or while handling the carcasses of dead animals. The disease may also be acquired by contact of the virus with the mucous membrane of the eye, the nose, or the mouth. This may happen by the animal snorting, by which small particles of pus or of mucus are blown into the face of an individual in attendance.

In making experimental inoculations with the secretion, placed in contact with the mucous membranes of animals, it has been found that considerable quantities of the material are necessary to ensure infection. This fact is accounted for by the small number of bacilli found in these secretions, they being easily destroyed by other bacteria. It is therefore often difficult to recognize the disease by a microscopical examination of the discharges from membranes or from abscesses.

The disease may also be transmitted from man to animals, and in very rare instances from man to man. Cases are reported where an entire family, one after another, has been attacked. It said to have been communicated by eating from the same dish with a diseased individual or by drinking from a pail which had been used by a diseased horse.

Bérard reports the inoculation of a medical student from a patient in the hospital, and more than one experimenter has fallen a victim to the disease during scientific inoculation-experiments. Man, in fact, appears to be highly susceptible to the disease.

Glanders in Man.—In 90 per cent. of the cases the disease is observed in individuals who come in contact with horses—coachmen, horse-dealers, soldiers, farmers, veterinary surgeons, students, and blacksmiths. According to Bollinger, only 6 out of 120 cases occurred in women, and these for the most part were employed in stables or belonged to the families of individuals thus employed. The period of incubation lasts from three to eight days (Korányi).

There has been a great variety of classifications, which, now that the etiology of the disease is understood, it is better to discard. The types of the disease, therefore, will simply be divided into *acute* and *chronic*.

At the end of the incubation period an inflammation appears at the point of inoculation, which inflammation frequently becomes severe and assumes an erysipelatous character, and an unhealthy ulcer forms. The adjacent lymphatic glands are swollen, and running toward them there are frequently red lines, indicating accompanying lymphangitis. Around the point of inoculation there appear often minute vesicles, which enlarge and become hemorrhagic, and which later suppurate or are accompanied by gangrene of the parts beneath. If the wound has already healed, it may reopen and ulcerate. This ulceration may eventually heal after a long time, or it may be followed by constitutional symptoms, leading to a fatal result without other local manifestations. Constitutional disturbance is, however, not always present, but there are often malaise, headache, and prostration, and more rarely a chill; but when the local inflammatory symptoms develop there is a corresponding amount of fever, which gradually subsides as the local symptoms improve and the patient recovers.

In the greater number of cases, however, the disease progresses farther. In the severe cases there are prodromal symptoms followed by an outbreak of fever. Nose-bleed is often an accompaniment of the fever; also severe pain in the muscles and joints, particularly in the lower extremities, but they may exist also in the neck and the chest; usually no swellings are seen at the painful spots, but at times there arise œdematous tumors, nodules, and boils, which may, however, disappear with great rapidity. Some of these swellings may suppurate and form abscesses.

After the fever has lasted from six to twelve days an eruption makes its appearance. Small papules, isolated or in clusters, form on the face, the trunk, and the extremities, and they gradually develop into pustules with an inflamed base. These pustules dry up or ulcerate while others are forming, and frequently bullæ appear with hemorrhagic or gangrenous contents. The face now begins to swell, either on account of the presence of pustules or from the condition of the nose. A dark bluish-red tumor forms, which is firm in consistency and which is covered with vesicles, presenting an appearance somewhat like that of the anthrax carbuncle. The eyelids are swollen and a thin muco-purulent discharge flows from the conjunctiva.

At first there is dryness in the nasal mucous membrane, and almost always there is hemorrhage. Later there is a feeling of tension about the root of the nose and the mucous membrane swells. The discharge at first is scanty, and is followed by a thin, tenacious bloody mucus, which later becomes a dirty yellow, and which is extremely foul in odor. Pustules and ulcers may be seen upon the mucous membrane, and perforation of the septum may occur. The discharge flows back into the throat, whence it may be expectorated.

Inflammatory changes also occur in the mouth, the pharynx, and the palate. The mucous membrane ulcerates, and the gums easily bleed. The breath of the patient becomes offensive; swallowing is difficult. In some cases the inflammation extends to the lungs and symptoms of bronchial catarrh occur. The expectoration strongly resembles that secreted from the nostrils. There may be pleuritic pains with difficulty of respiration, and occasionally œdema of the glottis supervenes. There is often gastric disturbance with symptoms of intestinal catarrh, and diarrhœa often occurs. In the mean time the development of pustules, boils, and abscesses continues, and suppuration may extend as deep as the muscles or even to the bones.

These different symptoms do not appear in any regular order. During the progress of the disease the patient becomes greatly weakened and the fever assumes a typical character. The pulse is rapid, but it becomes weaker as the disease progresses. Toward the end the skin is cold and clammy, the ulcers are much enlarged, and they discharge foul secretions. The evacuations are involuntary, and death may be preceded by coma or by tetanic convulsions.

The course of chronic glanders varies greatly: it may last months or even years, and many of the usual symptoms may be wanting. The same local changes in cases of inoculation may develop as those in acute glanders. In case no obvious primary lesion is visible, there may only be vague and ill-defined symptoms of debility, combined with recurring febrile attacks and pains in the limbs and joints. Presently a cough appears; there is tenderness about the root of the nose, with muco-purulent discharge mixed with blood; and the patient may finally waste away with symptoms of hectic fever. In many cases of chronic catarrh there may be considerable destruction of the septum and of other bones of the nasal passages.

When the cutaneous affections are a feature of the case there is less of the nasal catarrh. There are, however, numerous boils and abscesses, accompanied more or less with lymphangitis. The abscesses may break and discharge thick pus, and finally may heal or may remain as sinuses, discharging a thin, foul secretion. The favorite seats of abscesses are in the flexures of limbs, particularly of the lower extremities, and in the neighborhood of joints. The abscesses often become ulcers with everted borders. In addition to these abscesses there are often circumscribed or diffused swellings which are accompanied with considerable pain, but without much change in the skin, and which after a time disappear. The chronic form of glanders may continue indefinitely, appear to improve greatly, and then perhaps become acute, or the chronic symptoms reappear and the patient gradually succumbs to the disease.

Pathological Anatomy.—The characteristic features of this disease in man as well as in animals are the glanders nodules, or the so-called "farcy buds," which are found everywhere on the skin. Lesions are found also in the nose, in the subcutaneous and submucous tissue, in glands, in muscles, in the periosteum, and in bones.

In the skin the pustules are a characteristic feature. They are found to be due to a breaking-down of the corium and to the formation there of a cup-shaped depression filled with broken-down material. Appearing first like a flea-bite, the skin is raised in a papular elevation, on the apex of which the pustule develops; later the pustules are discolored by extravasations of blood, and, when the scales fall off, they may form ulcers. These ulcers evidently result from the breaking down of minute glanders nodules in the true skin. The nodules are seen also in the mucous membrane of the nose, and the changes here are so characteristic as to establish the diagnosis in doubtful cases. There is also catarrhal inflammation and ulceration, which condition may extend into the antrum and sphenoidal sinuses. In the later stages there is often extensive destruction of the bones, and the cranial cavity may be invaded, pus being formed beneath the dura mater.

Miliary nodules and little abscesses are found in the gums, the pharynx, the larynx, the trachea, and the bronchi, and there are found in the lungs numerous small areas of consolidation, some of which have suppurated.

The muscles also are frequently the seat of nodules. These nodules are found in the biceps, in the flexors of the forearm, in the rectus abdominis, in the pectoralis, and, finally, at the point of insertion of the deltoid. A species of capsule is formed by the inflamed perimysium, which capsule encloses nodules the size of a pea. Abscesses develop here also, and they may find their way to the surface through the skin or they may burrow down and cause necrosis of the bone. The synovial membrane is often studded with miliary nodules, and the cavity is filled with an exudation. The lymphatic glands are less affected in man than in horses.

There is also a fatty degeneration of the liver, a swelling and possibly infarction of the spleen, minute abscess of the kidney, and sometimes of the parotid gland. The testicle may become inflamed, and nodules with abscesses or fistulæ may eventually develop.

The *diagnosis of glanders* is often difficult, owing to the varieties of the disease and, in many cases, to the absence of an external point of entrance. When the constitutional disturbance has been profound the disease might at first be mistaken for typhoid fever. The presence of the multiple abscesses, both external and internal, makes up a picture which bears a striking resemblance to pyæmia. In both cases the presence of nasal symptoms, together with a consideration of the patient's occupation, would aid in the recognition of the disease. Some of the chronic types with implication of the lungs might readily be mistaken for tuberculosis, and the appearance at the autopsy even might in some cases be misleading. In the chronic form of nasal glanders the ozœna bears a close resemblance to the later stage of syphilis, and in some cases only by a course of scientific treatment might it be possible to make a differential diagnosis. The disease, however, can definitely be recognized by the demonstration of the bacillus and its culture, which on potato is most characteristic. As it is often difficult to obtain bacilli in the secretions, recourse must be had to inoculation of guinea-pigs in a manner presently to be described.

The *prognosis* of acute glanders is extremely unfavorable, the disease usually terminating fatally in from one to three weeks. In the chronic form, according to Bollinger, recovery takes place in about 50 per cent. of the cases. According to Korányi, the chronic variety, formerly known as "farcy"—that is, the nodular form—runs a more favorable course than the nasal form of chronic glanders.

The period of incubation of the *disease in animals* lasts from three to five days. The nasal form of glanders is more frequent in horses than in man. In the chronic form the catarrh of the nasal mucous membrane is usually one of the first symptoms, and an eruption of nodules in the membrane occurs at the same time. The disease may at first be confined to one side. An inspection of the nares will show the presence of nodules and ulcers. The submaxillary glands of one or both sides are enlarged. When the ulcers form, the discharge becomes purulent, and the disease gradually spreads from the nose through the air-passages to the lungs. Later, nodules or farcy-buds may appear beneath the skin. The animals gradually waste away, and they may ultimately die a year after the appearance of the first symptoms.

Acute glanders may occur primarily or it may come on at any time in the course of a chronic case. The disease begins with some febrile disturbance and with violent inflammation of the nasal mucous membrane. In a few days glanders nodules make their appearance in the nose, the throat, and the lungs. At the same time there is general engorgement of the lymphatic glands and lymphangitis. Nodules and cords are felt beneath the skin, which in places is œdematous. Swellings may subside suddenly and others appear at different points (flying farcy). These external symptoms show themselves at first about the head and the neck, and later they spread to other portions of the body. The animals begin to cough and to grow thin, and after an illness of from eight to fourteen days death occurs. The prognosis of the disease in animals is most unfavorable.

In a case of doubtful disease, whether in man or in animals, a bacteriological examination will settle the question of diagnosis. A small amount of pus from an ulcer or of the nasal secretion is spread over a cover-glass and stained by the ordinary method. When bacilli cannot be demonstrated in this way in the secretions, experimental inoculation may be made in animals for this purpose.

Straus recommends an inoculation of the secretions to be examined into the peritoneal cavity of guinea-pigs, or to obtain cultures from these secretions and then to inoculate the animals with these cultures. An inflammation of the testicles shows itself in the animal two or three days after the inoculation. The skin of the scrotum becomes tense, reddened, and shiny, and there is desquamation of the epidermis. An abscess eventually forms. These animals die in from twelve to fifteen days. The same symptoms occur after subcutaneous inoculation, but somewhat later.

Kalming prepared a mixture of a pure culture of the bacilli in water, and subjected it to a temperature of 120° C.; it was then filtered and injected into horses which were suspected of having glanders, and also into healthy horses. In the diseased animals it invariably produced a rise of temperature. Preusse and Pearson and others repeated these experiments with the same results. It may be concluded, therefore, that this substance (*mallein*) possesses a diagnostic value.

The *treatment* of glanders in man consists principally in the treatment of symptoms as they arise. If a wound is suspected of being infected with the virus, it should be allowed to bleed freely, and it should then be disinfected with a strong solution of corrosive sublimate or of carbolic acid, and be cauterized with the actual cautery. The external abscesses should be treated on antiseptic principles as far as possible. They should be laid open and thoroughly disinfected, and an attempt should be made in this way to arrest the progress of the disease. If the initial lesion is taken in time, such attempts may prove successful.

Bayard Holmes recommends thorough curretting, followed by swabbing the cavity with a saturated solution of sulphate of zinc. The cavity is then packed with iodoform gauze wet in a saturated solution of iodide of potassium. Excision of small nodules is recommended by him. In a case reported by Holmes a patient during two years and a half was anæsthetized twenty times, and new foci were opened or old ones scraped out. A permanent cure was finally effected. The strength of the patient should be maintained by judicious stimulation. The nasal ulceration may be treated by mild antiseptic washes and douches, and the condition in the mouth be treated by appropriate gargles. In acute cases there is little prospect of doing anything more than to relieve the sufferings of the patient.

The only approach to an attempt at a specific treatment of this disease is the employment of the so-called "mallein." It is prepared somewhat after the manner of Koch's tuberculin. Bonome prepares mallein as follows: A culture may be made from the blood or from the fresh viscera of animals who have undergone experimental inoculation with the virus, or from glanders nodules. The active principle of the glanders bacilli is precipitated by treatment with large quantities of alcohol. The fluid is afterward evaporated in a vacuum of 35° C. This first precipitate is dissolved in water, and is sterilized for three minutes at a temperature of 100° C., and is again precipitated and subjected to evaporation. In this way Bonome obtained, after the addition of sterilized water, a yellowish-gray, sometimes whitish, odorless, neutral fluid, which was preserved in a sterilized vessel with a 2 per cent. solution of carbolic acid.

Healthy guinea-pigs were not affected by the drug, but guinea-pigs which had been inoculated with the glanders virus were made worse by large doses of mallein (10–15 mg.), but were cured by repeated small doses (0.5 to 1.00 mg.). They thus gradually acquired immunity to larger doses. Rabbits wasted away and died from the effects of the mallein, their glanders being made worse. It was concluded, therefore, that mallein had a therapeutic value for guinea-pigs, but only a diagnostic value for rabbits. Mallein had only a diagnostic value for horses, producing fever in those that were affected with glanders. In guinea-pigs mallein appeared to act very much as tuberculin acts. These animals, when healthy, reacted to large doses of both drugs in the same way. In the case of glanders guinea-pigs react to small doses of mallein in the same way that tuberculous guinea-pigs react to small doses of tuberculin, minimal doses of these two drugs having a therapeutic value for these animals.

Bonome experimented also with cadaverin, thymus extract, and neurin. When these substances were mixed with cultures of the bacillus mallei they appeared to restrict its development, but the experiments made on animals do not appear to have been sufficiently complete.

Fortunately, epidemics of the disease do not flourish to any great extent in America. In Boston there have been six deaths from glanders in man during the years 1885 to 1891, inclusive. During 1891 there were but twelve cases of glanders in animals reported to the Board of Health. The animals were promptly killed, and the premises on which they had been stabled were thoroughly disinfected by the authorities. In the State of Massachusetts the regulations for the control of contagious diseases in cattle are made by the Board of Cattle Commissioners, and failure to comply with the law is punishable by fine or by imprisonment.

Epidemics of glanders were in 1887 reported to Washington, D. C., from the States of Georgia, Virginia, Texas, Pennsylvania, Louisiana, and the District of Columbia; also from Oowala, Cherokee Nation. The Minnesota State Board of Health reports that from March, 1885, to April, 1886, it had isolated over 450 horses affected, or suspected of having been affected, by glanders.

XXIII. SNAKE-BITE.

AMONG the great variety of bacterial poisons which have thus far been studied there is hardly one which can compare in virulence with the venom of poisonous snakes. It may be regarded as the acme of the type of animal poison, which in the rapidity and the disastrous effects of its action is without a rival.

Deaths from snake-bite are not very common in the United States, although rattlesnakes are still very numerous in certain portions of the country. In India, however, the mortality is frightful, which is due partly to the enormous number of serpents and partly to the careless habits of the natives and to the exposure of the person from scanty clothing.

A series of careful returns compiled by Fayrer shows that in 1869 the number of deaths from snake-bite in the Bengal Presidency was 11,416. He estimates that deaths in India from this source alone amount annually to 20,000. In 1881 the number of snakes killed for the bounty offered by the British government amounted to 254,968.

According to Yarrow, there are in America no less than twenty-seven species of poisonous serpents belonging to four genera. The first genus is the *Crotalus*, or rattlesnake; the second is the *Caudisona*, or ground rattlesnake; the third is the *Ancistrodon*, or moccasin, one of the species of which is a water-snake; and the fourth is the *Elaps*, or harlequin snake. There is also a poisonous lizard known as the *Heloderma suspectum*, or Gila monster.

In India, of the twenty-one families of snakes known to naturalists, four are poisonous; these are the *Elapidæ*, the *Hydrophidæ*, the *Viperidæ*, and the *Crotalidæ*, and they are known by the appropriate name of *Thanatophidia*.

Among the Elapidæ, of which there are five species, is the *Naja tripudians*, or cobra. It is a most deadly snake, and it is found in many parts of India. It grows to the length of 5½ feet or even more. It is most active at night, but it is often seen moving about during the day. It is, like the *Ophiophagus*, a hooded snake. The Ophiophagus, another species of this family, is probably the largest known venomous snake, growing to the length of from 12 to 14 feet. It is not only very powerful, but is also very active and aggressive.

The Hydrophidæ, as their name implies, inhabit the salt-water estuaries and tidal streams. They are all venomous, and are very poisonous.

The Viperidæ, which are terrestrial snakes, are more poisonous than the Crotalidæ. The latter genus has not, as has its American namesake, a rattle, and it is less poisonous; it is also a smaller snake, measuring about 3 feet in length, the American snake reaching at times the length of 5 or 6 feet.

The heads of these serpents are so constructed as to admit of a large amount of movement in the component bones. The superior maxillary bones are united by ligaments only to the intermaxillaries, and the lower maxillary bones are so arranged as to be separable from one another anteriorly and to permit motion of one side only if desired. The mobility of the superior maxilla is essential to the movements of the fang, which is firmly attached to it. This fang, in the rattlesnake, is sometimes quite large, measuring three-quarters of an inch in length. In the cobra it is decidedly smaller. In the rattlesnake the fang is somewhat conical and scythe-shaped and has a sharp point. It has a deep groove, due to the folding of its edge, which gives it the appearance of being hollow. The fang communicates with the duct of the poison-gland, which is situated behind the eye and beneath the anterior temporal muscle. The walls of the duct are supplied with an unstriped muscular fibre forming a sphincter muscle, which enables the serpent to control the discharge of the fluid. The duct-opening lies at the base of the tooth, where it communicates with the fissure in the fang. In the pulp-sac in the jaw lie the nerve-fangs, and when the fang is lost by a natural process it is replaced within a few days; but when violently removed the new fang does not appear for several weeks. When in repose the fang is folded back and covered by a fold of mucous membrane which retracts when the fang is erected.

The amount of venom contained in the gland varies greatly: when perfectly fresh and healthy the snake throws out at first from ten to fifteen drops. But if the snake has recently excreted the fluid, only three or four drops can be obtained from the glands. The color of the venom of the rattlesnake varies from pale emerald-green to orange- or straw-color, and it is more or less glutinous in consistency. In the Indian snake it is a clear viscid fluid, soluble in water and slightly acid in reaction. It is equally virulent whether dry or preserved in alcohol or in glycerin. The active principles of the virus have been found by Mitchell and Reichert to consist of two proteids, a globulin, and a peptone. Prolonged boiling seems to convert the peptone into a coagulable albuminoid which is not destructive to life.

It is generally supposed that rattlesnake poison, if swallowed, is harmless, but, according to Fayrer, the poison of the cobra can be absorbed through the mucous membrane, though with much less dangerous effect than when it is introduced into the blood: Mitchell and Reichert state if enough of the poison is taken into the empty stomach death may ensue. According to Mitchell, the venom exerts a powerful local effect upon the living tissues, and induces more rapid changes than any known organic substance. It renders the blood incoagulable, and it so acts upon the capillary blood-vessels that their walls are unable to resist blood-pressure, thus allowing the corpuscles to escape into the tissues. The swelling produced is not due to inflammation, but is due to hemorrhage. The bodies of the red blood-corpuscles lose their shape and fuse together into irregular masses, acting like soft elastic colloid material.

Death occurs, according to Mitchell, through paralysis of the respiratory centre, paralysis of the heart, hemorrhages into the medulla, and possibly from the inability of the red corpuscles to perform their functions. Cobra-poison does not produce the marked lesion of the crotalus-poison, because it is lacking in globulin.

Fayrer states that the poison acts through the circulation upon the nerve-centres, paralyzing them and thus destroying the vital force. The experiments made by him and Brunton also show impairment of the respiratory centre.

According to Feoktistow, whose experiments were performed at Dorpat, the poison acts solely on the nerve-centres, and it has no effect whatever upon the blood. According to Wall, the symptoms of cobra-poisoning are due to a slowly-advancing general paralysis, death being caused by convulsions due to asphyxia, the poison acting upon the respiration. The effect of the cobra-poison on the blood, he thinks, is not great. It will thus be seen that European observers dwell more upon the action of the virus upon the nervous system and less upon the blood.

The mechanism by which the act of striking is accomplished, and by which the virus is thrown into the system, is thus described by Yarrow: "The snake prepares for action by throwing itself into a number of superimposed coils, upon the mass of which the neck and a few inches more lie loosely curved, the head elevated, and the tail projecting and rapidly vibrating. At the approach of the intended victim the serpent by sudden contraction of the muscles upon the convexity of the curves straightens out the anterior portion of the body and then darts forward the head. At this instant the jaws are widely separated, and the back of the head fixed firmly upon the neck. With the opening of the mouth the spheno-palatines contract, and the fangs spring into position, throwing off the sheath as they leap forward. With the delivery of the blow and penetration of the fangs the lower jaw closes forcibly, the muscles that execute this movement causing simultaneously a gush of venom through the tubular tooth into the wound." As the serpent withdraws his head the fangs are forced more deeply into the tissues, and the jaws are finally loosened from their hold by a shaking movement of the head, which liberates the teeth. The wound is inflicted by the rattlesnake, in almost every case, upon an extremity. In India, according to the reported cases, the patient is often struck upon the shoulder or the neck.

The *symptoms* vary greatly according to the severity of the wound inflicted. Many cases recover simply because a complete inoculation has not taken place, but when the act has thoroughly been accomplished in the way above described, and the hypodermic injection of a full dose of virus has occurred, the sequence of events follow in a characteristic and almost inevitable course. The pain in the wound varies greatly. Sometimes it is hardly observed; at other times it is described as a sharp, stinging pain. In most cases the wound is more or less painful. The puncture is sometimes so small as to be hardly perceptible. The succeeding local symptoms are swelling, discoloration, and increasing pain. This swelling is regarded by Mitchell as not due to inflammation, as described by several writers, but to the effusion of blood. If the progress of the poison has not been arrested by a ligature after a period varying from minutes to hours, the swelling and discoloration extend up the limb, accompanied by severe pain. Vesicles soon form, and the disorganization of the tissues is so rapid that the part becomes gangrenous if the patient survives long enough. The direful effect of serpent-poisoning upon the tissues is graphically described by Lucan (*Pharsalia*, book ix.), who records the somewhat exaggerated stories of Cato's soldiers in their march through the Libyan desert. (This passage is also interesting as being probably the first occasion in which the peritoneum is mentioned in poetry.)

> Wretched Sabellus by a seps was stung;
> Fixed to his leg with deadly death it hung:
> *   *   *   *   *   *

Of all the dire destructive serpent race,
None have so much of death, though none are less.
*   *   *   *   *   *
The spreading poisons all the parts confound,
And the whole body sinks within the wound.
The brawny thighs no more their muscles boast,
But, melting, all in liquid filth are lost;
The well-knit groin above, the ham below,
Mixed in one putrid stream together flow;
The firm peritoneum, rent in twain,
No more the pressing entrails could sustain;
It yields, and forth they fall; at once they gush amain.

The necessity for prompt action was recognized, as is shown by the experience of Murrus:

Along the spear the sliding venom ran,
And sudden from the weapon seized the man:
His hand first touched, ere it his arm invade,
Soon he divides it with his shining blade:
The serpent's force, by sad example taught,
With his lost hand his ransomed life he bought.
(Rowe's translation.)

The constitutional symptoms of crotalus-poisoning do not appear immediately, but after an interval of a few minutes or of hours there is prostration of the most severe character. In the case of cobra-poisoning a considerable interval of time—one or two hours—has been reported before the advent of constitutional disturbance. There is sometimes reported a feeling of intoxication or of elation, but this is rare. Some of the early symptoms are probably due to fear. The patient, after walking some distance, feels his limbs give way beneath him, and he staggers and falls. The skin is bathed in a cold, clammy sweat; the expression is anxious; the pulse becomes rapid and feeble. The breathing is usually hurried and is more or less labored. In some cases it is diaphragmatic. The patient sometimes complains of a pain in the chest and a sense of suffocation. Foaming at the mouth is occasionally observed. Ewart speaks of the breathing becoming slower and slower as death approaches, but this is probably in the last stages of coma. If the patient lives long enough, the local swelling and discoloration of the arm continue to increase, and they may spread on to the chest and back.

The *pathological changes* found upon man after death seem chiefly in the brain and its membranes. In Fayrer's cases congestion of vessels on the surface of the brain is reported, and there is occasional softening of the cerebral substance. The latter may, however, have been due to a post-mortem change, which would occur rapidly in the Indian climate. Fluid was often found in the lateral ventricle. The pia mater is reported as engorged in several cases. In Horner's case, reported by Mitchell, the brain was found to be of a healthy consistence, but so congested that the cortical substance was of a deep brown tint. A drachm of transparent serum was found in each lateral ventricle. The veins of the pia and the vertebral veins were full of blood. In two other cases recorded by Mitchell the same conditions of the brain were found.

In some of Fayrer's cases the lungs were reported as congested, and dark sanious fluid was occasionally seen flowing from the mouth, but in many the lungs appear to have been quite normal. In one of the cases quoted by Mitchell the walls of the trachea and the bronchial tubes were congested and the trachea and bronchi were full of a frothy mucus.

As regards the stomach and intestines, congestions of the mucous membrane were occasionally reported, but more frequently they were found to be normal. No pathological changes appear to have been found in the great majority of the cases in the liver, the kidneys, or the spleen. The blood in almost all cases is found to be fluid and non-coagulable.

The changes in and about the wound vary greatly from infiltration by a dirty-brown serum or extravasations of blood to extensive disorganization. Fayrer reports in one case that when the left hand was cut into, the muscles were found disintegrated and of a dark color, and in the upper arm the muscles were found to be soft and infiltrated with serous effusion. In Sir E. Homes's case, reported by Mitchell, a large abscess existed in the arm and forearm, and the cellular tissue between the muscles had sloughed extensively.

After experimental inoculation in animals Mitchell found the tissues around the point of injection soaked with extravasated blood, and if death had been postponed for some length of time, the tissues at some distance from the point of injection were also affected in this way to a certain extent, but not so extensively. Pronounced and frequent ecchymoses were found beneath the serous membranes, and there was general congestion of the blood-vessels throughout the body. The blood coagulated imperfectly, and then only after being exposed to the air, "resembling in this particular the state of that fluid observed in conditions of asphyxia."

In no form of disease or injury, except hemorrhage from the great vessels, is *promptness of action* so important. The first thing to be done is the application of a ligature. Every minute, even every second, is of value, because in many reported cases life seems to have been saved chiefly by the prompt application of the ligature. It must be applied tightly. The clothing, a piece of twine, anything at hand, should be used for this purpose, and a second ligature, broader than the first, may be applied higher up on the limb. A stick may be inserted into the top of the ligature to twist it, so that an improvised tourniquet may be formed. The bites should then be laid open and an effort be made by cupping or by suction to withdraw the venom from the tissues. A more effective way of accomplishing the removal of the virus before it has had time to spread is an excision of the part in which the venomous fluid lies. A portion at least of the poison is thus certainly removed and the dose correspondingly diminished. It is recommended to wash the wound with a 1 per cent. solution of permanganate of potash or of aqua ammonia. The use of the actual cautery is probably more efficient, as it is only by intense heat that the virus seems to be destroyed, experiments having shown that the permanganate and the ammonia are not to be depended upon to affect its virulence. It is the custom of Indians and hunters to flash powder on the wound for this purpose. An ember of hot coal would be more efficient still.

If the bite is not on an extremity, the injured skin should be cut out ruthlessly by any one present. The danger of bleeding would probably be slight in any case. Care should be taken not to expose the open mouth of a vein or a serous sac to the venom.

The use of stimulants still holds its popularity, and the whiskey cure is to-day probably the one most resorted to in the United States. As prostration is one of the most prominent symptoms, the use of alcohol is undoubtedly indicated to strengthen the flagging heart. It should, however, be given in moderation at first, particularly in the young, as it is not improbable that some patients have actually succumbed to the heroic nature of the treatment.

As the ligature cannot be allowed to remain permanently for fear of gangrene, it must be released momentarily from time to time. It is at this period that the alcoholic stimulant will be of advantage to sustain the strength of the patient, as fresh doses of the venom are thus unavoidably allowed to work into the system. A careful watch upon the pulse will be the guide for treatment.

A great variety of drugs have been recommended from time to time, and have eventually proved to be worthless. Lacerda of Rio Janeiro found that an injection of a 1 per cent. solution of permanganate of potash into the wound of an animal that had been inoculated was an absolute antidote. The remedy has been tried with varying success. The use of aqua ammonia has also had its advocates, and this drug was at one time supposed to be a specific in its action upon the venom. As a cardiac stimulant it has undoubtedly done good work, but no more decided benefit can now be claimed for it. The gall of serpents, "snake-stones" (a fragment of bone washed in blood, dried, and polished), and a great variety of other local remedies are mentioned in the literature of this subject.

It is probable that many cardiac stimulants might be used with advantage, such as nitro-glycerin, digitalis, and strychnine. Dr. Mueller of Sydney, Australia, has recently published a monograph advocating enthusiastically the use of large doses of the latter drug given subcutaneously, basing his method on Feoktistow's theory of the action of the poison on the nerve-centres. He recommends that as much as $\frac{1}{2}$ a grain of strychnine should be given in divided doses, 16 minims of the liquor strychniæ (P. B.) being injected at a time. If under these large doses the symptoms abate or if the latter are comparatively mild at first, smaller doses should be injected, as $\frac{1}{15}$ or $\frac{1}{10}$ of a grain; but under all circumstances the rule that distinct strychnia symptoms must be produced before the injections are discontinued should never be departed from. Many cases apparently at the point of death seem to have been revived and finally cured by this treatment. It has, however, met with much adverse criticism in Australia, and has had thus far only a very limited trial in India. Calmette has studied the serum of animals rendered immune to the venom of serpents. According to this observer, animals can be rendered immune in two ways: either by repeated injections of venom of full strength in very small and gradually increasing doses, or of venom which has been modified by combination with chloride of gold or chloride of lime. The serum of animals thus treated has also an immunizing and antitoxic action. This action exerts itself not only when brought in contact with the venom with which the animals in question have been previously treated, but also with the poison of other serpents. It was found that the serum of a rabbit that was immunized by cholera virus exerted an antagonistic action to the venom of the French viper and that of several Australian serpents.

Calmette found that 4 ccm. of antitoxic serum, injected into a rabbit an hour and a half after 1 mg. of cobra-poison had been injected into the same animal, was sufficient to save the animal. In rabbits which had not received the serum death occurred in twelve hours after the injection of 1 mg. of the cobra-venom.

If the poisoned animal was treated with chloride of lime, a cure was effected without resort to the serum. The solution, which is of the strength of 1 to from 12 to 45 parts of water, should be injected in doses of 5 ccm. subcutaneously around the wound. From 20 to 30 ccm. of a more dilute solution may be used in the same way. This method, when employed twenty minutes after inoculation with the venom, saved animals which would otherwise have died in two hours.

Whatever the treatment may be, the patient should be kept quiet. All his spare strength should be kept in reserve. He should be encouraged and soothed. Hot bottles may be applied to the heart, and the general rules for the treatment of shock might well be resorted to with advantage.

It is most important to remember, in estimating the value of any particular line of treatment, that a careful estimate of the dose of the venom should be made in each case, for in inflicting the injury the serpent often fails to accomplish its purpose, and only a drop or two of the poison may come in contact with the exposed tissues.

XXIV. TUBERCULOSIS.

Tuberculosis did not until recently especially interest surgeons, but it now covers a large field in surgical pathology. The surgeon has, in fact, more to do with the disease to-day than the physician.

The inoculability of tuberculosis was first recognized in 1826 by Laënnec, who became infected by an injury to his finger from a saw during an autopsy upon a case of disease of the vertebræ. Eventually he died of phthisis.

Villemin in 1865 was the first, however, to demonstrate experimentally the possibility of transmitting the disease from man to animals. He showed that the cheesy products of tuberculous inflammation when introduced into the tissues of rabbits and guinea-pigs produced a miliary tuberculosis. He, however, did not identify the microscopical characteristics of the new formations thus produced with tubercle, nor did he undertake to show that other products might not produce the same results. Cohnheim and others, however, endeavored to show that any cheesy material, whatever its origin, would produce the same appearances of tuberculosis when inoculated.

It was attempted also to produce tubercular nodules by introducing different kinds of foreign bodies into the tissues. But, although minute tubercles closely resembling the genuine tubercle were thus produced, yet they did not appear capable of spreading to distant organs or of being transmitted from one individual to another.

The recognition of the characteristic giant-cells and epithelioid cells of tubercle, and of the tendency of the tubercular masses invariably to undergo cheesy degeneration, helped to throw light upon the investigations which were then being made.

Cohnheim, whose experiments on the cornea enabled him to study the development of the tubercle after inoculation, found that a considerable space of time intervened between the inoculation and the development of the disease—that, in other words, there was a distinct period of incubation.

A great variety of experiments followed. Tuberculous peritonitis was produced by the injection of diseased sputa into the peritoneum of guinea-pigs; infected food was proved to produce ulcerations of the intestinal canal and the subsequent involvement of the mesenteric glands; the dried sputa, when inhaled, produced pulmonary tuberculosis. The old belief that tuberculosis was caused by a weakness of the tissues gradually yielded to the conviction that it was a genuine infectious disease. These views received their confirmation in the discovery of the bacillus of tuberculosis, and in the demonstration by Koch that by it alone could the phenomena of the disease be produced.

Koch's discovery in 1882 fairly revolutionized a great department of surgery. He made his first observations of the bacillus of tuberculosis in the expectorations of phthisical patients and in sections taken from miliary tubercles. He succeeded, also after many trials, in producing a culture of the bacilli on blood-serum, his skill as a bacteriologist enabling him to overcome the unusual difficulties that surrounded the cultivation of the organisms. With these pure cultures he made a series of inoculation-experiments upon rabbits, guinea-pigs, and field-mice, introducing the virus subcutaneously or into the various cavities of the body, and also by intravenous injections, and in this way he was able to obtain acute miliary tuberculosis. The tubercles taken from such animals contain large numbers of bacilli, and they are much better suited for microscopical examination than the specimens taken from human subjects. From these animals, finally, he was able to reproduce the cultures, and then to establish fully the identity of the organisms with the disease.

The bacillus of tuberculosis, which is a thin, staff-shaped body from 3 to 4μ in length, will be found more fully described elsewhere. The *submiliary tubercle* is the pathological structure from which are developed the tubercular nodules found in diseased organs or in tissues. It is composed of a globular mass of small round cells, in the centre of which mass is found one or more giant-cells. The giant-cells, which are a very characteristic feature of the miliary tubercle, enable one to make an almost positive diagnosis even when no bacilli have been discovered. The peculiarity in this form of giant-cells consists in the arrangement of the nuclei, which are found chiefly in the periphery, arranged with their long diameters radiating from the centre of the cell. At the centre there is more or less evidence of a degenerative process. Surrounding this cell are seen one or more large cells rich in protoplasm, with large nuclei and nucleoli, which are known from their size and appearance as *epithelioid cells*. According to Cheyne, the epithelioid cells are the most characteristic, as they are more constant than the giant-cells. They are, in his opinion, more frequently the seat of the bacilli which lie between them. These cells may be derived from the epithelium, as, for instance, in the lung, or from the endothelium of a vessel, or from tissue-cells. They are more numerous at the periphery of the tubercle.

The remaining cells of the tubercle are round or are slightly spindle-shaped, and the cell-cluster is supported in a fine reticulum of connective tissue which in some cases is quite dense at the periphery (Fig. 76). The bacilli are found scattered here and there

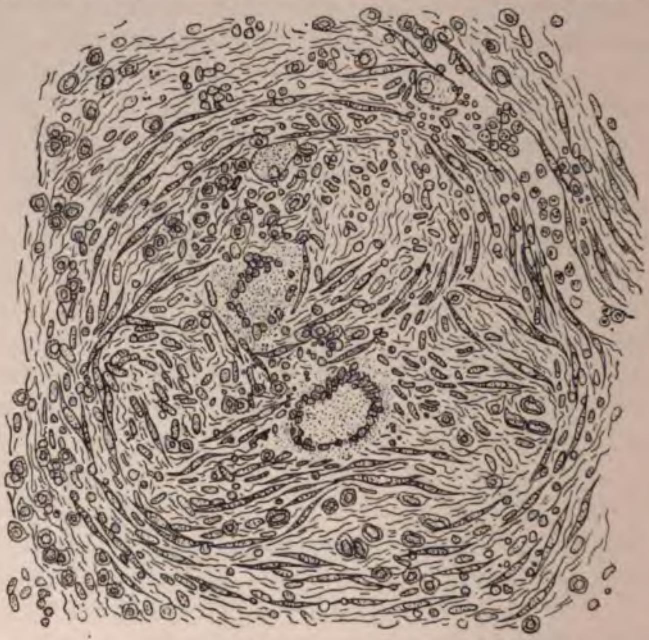

FIG. 76.—Submiliary Tubercle, showing giant- and epithelioid cells. The prevalence of the spindle is probably due to the locality (the tongue) from which the specimen was taken.

in varying numbers between the smaller cells, and also in the body of the giant-cell. In the experimental forms of miliary tubercle the bacilli are usually very numerous, and they are then seen, in stained specimens, forming an ornamental border near the fringe of nuclei in these large cells. Very few are found in the interior of the cell. In pathological tubercle in the human subject it is not at all an easy matter to find bacilli, and several specimens are often searched through with great care before a single bacillus is discovered.

In infiltrating tubercle the epithelioid cells are not collected in small clusters, but are seen through the tissue in broad tracts, or they are simply scattered irregularly among the other tissue-elements. The tissue which is the seat of the infiltration presents two chief types—namely, granulation tissue and gray fibrous tissue. The latter type shows less tendency to break down (Cheyne).

The origin of the cells of the tubercle has been a subject of much dispute. According to Baumgarten, the cells found in the early stages of the development of the tubercle are not leucocytes, as has been supposed, but they originate by the process of indirect cell-division from the fixed cells of the part, whether they happen to be of connective-tissue origin or are derived from the epithelium of a gland or from the endothelium of a minute blood-vessel. The giant-cell does not develop from a fusion of several epithelioid cells, but it is the product of the nuclear proliferations of a single cell. Under the moderately stimulating action of the tubercular virus the cell does not receive sufficient irritation to undergo proliferation. The protoplasm remains, therefore, undivided and increases in size, while the nuclei continue to accumulate in large numbers. In many cases of very acute tuberculosis, for this reason, giant-cells are not to be found. The centre of the cell is without nuclei, as the protoplasm has here already begun to undergo that change so characteristic of the disease—namely, cheesy degeneration. After the virus has thus affected the fixed cells of the part, it produces also an irritation upon the walls of the small vessels; consequently exudation takes place, and the tissue is found infiltrated with leucocytes, but this occurs usually in a later stage of the development of the tubercle.

The reticulum of fibres in which the cells lie is not usually a new formation, but is merely the remains of the pre-existing intercellular substance. As the cell-growth is most active at the centre of the mass, and a certain pressure is thus exerted from within outward, there is seen at the periphery a thickening of this network amounting at times almost to the formation of a capsule. In some cases the reticulum seems to be formed, at least to a large extent, by the processes of the epithelioid cells. The vascular supply is usually very slight, the smaller vessels disappearing altogether. The consequence is, that the vitality of the diseased mass is soon affected, and an anæmic necrosis occurs, which, accompanied by a granular disintegration and a fatty degeneration of the cells, produces the condition known as *cheesy degeneration*, which is found in the middle of the nodule, and which may gradually extend so as to affect the whole mass. The bacilli also appear to exert an influence which brings about a chemical change in the cells. The nuclei disappear, the cells refuse to take any coloring reagents, and coagulation-necrosis takes place. The result of these changes is the formation of a mass of dead tissue and of cheesy débris in the centre of the tubercle. Where this formation is extensive ulceration, or even abscess-formation, may take place. Occasionally lime-salts may be deposited in these central portions of the tubercle, resulting in calcification. The tubercle may be surrounded by a well-marked zone of granulation tissue, or the tissue of the tubercle may pass into the surrounding tissues without any well-marked line of demarcation. A dissemination of tubercle can take place only when the original focus is broken down and in a state of ulceration. When inflammatory reaction occurs around the tubercle, incapsulation may take place, and the system may in this way be protected from invasion.

The *entrance of the tubercular virus into the body* is through various channels. The question of the transmission of the disease from mother to child through the placenta has been much discussed since the discovery of the bacillus. Baumgarten is one of the most prominent advocates of this source of the tubercular virus, and, according to this investigator, it may be received during fœtal life only to manifest itself perhaps many years later. Tuberculosis of new-born infants is, however, an exceedingly rare occurrence, and in the reported cases of early tuberculosis the possibility exists of the acquisition of the disease from the breast of the mother or in other ways. It is true that there are recorded cases which illustrate the possibility of such transmission from animal to animal. Cornil reports the case of a fœtal calf whose lung contained a tubercular nodule. The fœtus was taken from the uterus of a tuberculous cow. Inoculation experiments on pregnant guinea-pigs have not, however, been successful.

Hereditary tuberculosis, then, is an occurrence so extremely rare that it cannot be regarded as one of the ways in which the disease is acquired by the human subject. Many authorities still maintain, however, that a predisposition exists which may have been inherited—that in certain families the tissues and fluids of the body furnish a more favorable soil for the growth of the bacillus. The difference in susceptibility to the virus may be the same in different individuals as it is in different kinds of animals. Fränkel does not accept even this possibility, although he admits that a delicate constitution and a catarrhal condition of the air-passages, with feeble respiratory action, would present conditions favorable for infection. It is generally found that tuberculous patients have a family history of tuberculosis. Certain individuals, however, are peculiarly exempt. It is well known that nurses in attendance upon the sick in hospitals for consumptives may remain there years without infection, and that surgeons constantly wound themselves with tuberculous bone without danger. The family physician will tell you that in his private practice he rarely sees tuberculosis in healthy families. It is probable, therefore, that a predisposition to tuberculosis is inherited by children from their parents, but the disease must nevertheless be looked upon as one which is acquired during life by infection.

Probably the most frequent route through which the virus is introduced into the body is through the lungs. The durability of the organism and its power to retain its vitality in the dried state make possible its introduction with the inspired air. The expectorations of consumption, therefore, are a source of danger, as has abundantly been shown, not only when injected experimentally into animals, but also when allowed to dry upon the carpets or the linen. Cornet has shown that the dust of rooms occupied by such patients contains an abundance of the bacilli of tuberculosis, and Prudden and others have also found them in the dust of the streets. If the sputa are preserved in a moist state, the bacilli are imprisoned, and hence do not become a source of danger.

When introduced experimentally by inhalation, broncho-pneumonia is produced at the extremity of the tubes, and the bronchial glands become infected later. According to Bollinger, not every tubercular disease of the lung is due to the inhalation of the virus, for it may occur there secondarily by metastasis. It is, for example, a well-known clinical fact that caries of the wrist is very often followed by pulmonary tuberculosis.

Contagion may take place also through the digestive tract. It may be transmitted from mouth to mouth by a kiss, or by the spoon or the glass used by the consumptive. It should not be forgotten that the spatula or the dentist's instruments may, if not properly disinfected, become a source of danger to the patient. The susceptibility of the mucous membrane is increased by inflammatory processes, such as rhinitis and pharyngitis, and the virus may thus be transmitted to the submaxillary and cervical glands. The intestinal canal of animals is readily infected by tuberculous food. In man is found also primary tuberculosis of the intestine from vitiated food. The milk of tuberculous cows is now a well-recognized source of danger. Water may also be the vehicle of the virus, experiments in Cornil's laboratory showing that the bacillus could live seventy days in sterilized Seine water of the ordinary temperature.

Even meat that has been roasted may be a source of danger, for the central portions may not have been subjected to a sufficiently high temperature. Secondary tuberculosis of the intestine depends upon auto-infection, the sputa often being swallowed. The membrane of the bacillus is sufficiently tough to withstand the gastric juice; consequently the bacillus arrives unaltered in the intestinal canal, where it attacks Peyer's patches and the solitary follicles. The mesenteric glands are subsequently affected, and tuberculosis of the peritoneum may thus be developed, particularly in man. In women, however, the peritoneum is more frequently infected through the urogenital tract. As the result of such infection tuberculous peritonitis occurs. Infection through the skin is, according to Bollinger, underestimated, although the bacilli do not appear to be able to enter the pores of the skin like the pyogenic cocci. Tscherning reports the case of a servant who cut his finger while cleaning the spit-cup of his master, a consumptive. There formed a small cutaneous ulcer, which afterward became a nodule: a few months later the finger and the tendons of the palm of the hand became swollen and the cubital and axillary glands were enlarged. The finger was amputated and the glands were excised, and they were found to be tuberculous. The patient remained well. Middledorff reports the case of a man who wounded his knee-joint with a cutting instrument, and bound the wound with his handkerchief, which probably contained dried sputa. Two weeks after the accident the knee began to swell and excision of the joint for white swelling was ultimately performed. An examination of the tissues showed the presence of bacilli.

"Anatomical tubercle" is an example of infection received by those who are in the habit of handling infected bodies. Cheyne reports a case of a student who injured the fold of the nail at an autopsy. A wart formed, which remained as an ulcer after three years of treatment: an abscess on the back of the hand finally formed, and the finger was amputated. Death from tubercular meningitis occurred six years after the injury. The oft-quoted example of infection of the prepuce in the rite of circumcision by the mouth of the operator, who was tuberculons, is another instance.

Certain portions of the body appear more easily infected than others: the face and the head are peculiarly liable, and even certain organs and tissues appear to be predisposed. Many inflammatory skin affections, which are at first purely benign, may subsequently become tuberculous.

No example of infection with tuberculosis during vaccination has been reported: it is probable that the bacilli are unable to live in the vaccine lymph. Lawrence, indeed, reports two instances of remarkable recovery from advanced stages of tuberculosis after an attack of small-pox of a virulent type.

Cases are reported of tuberculosis of the internal organs of generation, which cases, it is possible, may have been due to infection during coitus.

A large number of tuberculous diseases owe their origin to intravascular infection, the virus gaining an entrance at some unknown point. Thus, it may appear first in a chain of glands, as in the neck, or in some portion of the osseous system.

Acute infectious diseases, like measles and scarlet fever, often pave the way for tuberculosis. Susceptibility to the disease is not the same at all periods of life. Individuals who have been the subjects of tubercle in youth often enjoy a particularly healthy existence in later life.

The tuberculous process may spread in different ways and by different routes. The original nodule may invade the neighboring parts by a simple process of growth. Distant portions of the body are reached usually through the lymphatic system. The lymphatic glands, however, exert a protective influence: they may not only retard the advance of the bacilli, but may also be indirectly the cause of their destruction. When the last of a chain of glands has been traversed the bacilli are conveyed through the thoracic duct into the general circulation. A thrombus may form in a vein adjacent to a tuberculous nodule, and metastatic foci may be established through embolism, or the wall of a large vein may become involved by invasion of the virus from a neighboring nodule, and bacilli may then be let loose into the circulation. They are conveyed eventually to some arteriole or capillary, where they become attached to the endothelium, and the conditions favorable for the development of a miliary tubercle are established. In this way acute miliary tuberculosis may occur.

The disease may also spread by an invasion of an adjacent serous sac, by the growth of the nodule, or by suppuration, and it may discharge into the sac. If the integrity of the sac is still maintained, it will be in communication with the lymphatic system, and the danger of dissemination will be much greater than when the membrane has changed into a wall of granulation tissue which has blocked up the lymphatics. When the bacilli gain access to cavities lined with mucous membrane, such as the bronchial tubes or the intestines, they pass over long surfaces, increasing the opportunity for infection.

Tuberculous affections are apt to be multiple. The multiple form may occur in the primary stage of the disease, as in spina ventosa, where several fingers are usually involved, or there may be separate infections at different times. A familiar example is that of a patient who had scrofulous glands in childhood, later had white swelling of the knee, and eventually died of pulmonary tuberculosis. It is probable that in a case such as this the different manifestations have some connection with one another, and that they are examples of periods of latency of the disease followed by metastatic deposits.

The original tubercular focus may, however, be absorbed in consequence of the influence of the inflammatory process which has been set up around it. The tubercle becomes encapsuled. The cells undergo cheesy degeneration or calcification, and cicatricial tissue finally occupies the seat of the tubercle; or ulceration of the neighboring parts occurs and the tubercle is thus removed. If any bacilli remain behind, there is always danger of a renewal of the tubercular process, as the organisms are exceedingly tenacious of life, and either they or their spores, if such exist, may be able at a favorable moment to begin again an active development. The danger of relapse in this disease, therefore, is always great. Miliary tubercles may be found in nearly every portion of the body. They develop readily in the connective tissue, in or around minute blood-vessels, in the parenchyma of organs, or on the surface of membranes.

Tuberculosis probably affects more individuals than any other form of infectious disease, for it has roughly been estimated that out of every five deaths one is due to this cause. Notwithstanding a very large proportion of those affected recover their health, it will readily be seen that the bacillus of tuberculosis is one of the greatest scourges of the human race.

In 384 autopsies of children who died of acute infectious disease in a hospital in Copenhagen between 1884 and 1887, 198 showed undoubted evidences of tuberculosis. Almost without exception these children had no sign of the disease during life: in all cases the disease occurred in the lymphatic glands.

In the Medical Institute of Munich, in 500 autopsies on children under fifteen years of age, tuberculous disease was found in 150 cases. In other words, 30 per cent. of those who died at that hospital were tuberculous. Statistics of the autopsies performed upon adults in that city during a period of nearly thirty years, a city renowned for the stringent rules in regard to the examination of the dead, showed that tuberculosis existed in 29.4 per cent. of the cases. It is found, therefore that, although not always the cause of death, tuberculosis existed in one-third of those who died during a very considerable period of time.

Tuberculosis of Bone.—One of the commonest of tuberculous diseases, and one of great importance for the surgeon to understand, is tuberculosis of the bones and joints. Common as this affection is, it is nevertheless one which suffers greatly from the ignorance and indifference of many who are called upon to treat it. The great advance in the knowledge of its pathology has placed the surgical treatment on an entirely new basis, and the extent and limitations of tubercular bone disease and the possibilities of intelligent operative interference are not yet fully appreciated.

Tuberculous disease of bones and joints, in the great majority of cases, follows slight contusions and sprains. Spondylitis, or Pott's disease, usually occurs, in a susceptible individual, after a fall or a sprain. A bruise of the spongy tissue of one of the bodies of the vertebræ or of the head of the tibia, or in one of the tarsal bones, is followed by a laceration of some of the delicate vessels of the spongy tissue, and an effusion of blood consequently takes place between and around the cancelli of bone or into the synovial cavity of a joint. The result of such an injury impairs for the time being the nutrition of the part affected, the circulation does not go on so actively, and there is a period during which absorption of the effused blood and exudation does not take place. The point of injury and the surrounding tissues are momentarily disabled by the damage that has been done, and they are in a less resistant state to the invasion of bacterial poison. Individuals predisposed to tuberculosis may already have, as has been shown, the seeds of the disease temporarily imprisoned in the lymphatic gland. The bacilli may reach the injured spot as single organisms floating in the blood, and thus find ready access to the extravasated clot through the open mouth of the blood-vessels; more rarely they may reach the region in the interior of an embolus which may have become detached from a degenerating gland that had discharged its contents into a vein, or which may have communicated with the pulmonary capillaries, and thus have directed the embolus into the arterial system. When such an embolus is caught in a terminal artery, wedge-shaped infarctions and wedge-shaped sequestra are not uncommon in the articular extremities of long bones. These light forms of injuries are a more frequent source of tuberculosis than are more severe accidents. The French government at one time called attention to the large number of cases of amputation for tuberculosis of the ankle-joint following sprains, and enjoined special care in the treatment of this injury. All writers bear testimony to the fact that it is extremely rare to find tuberculosis of the bone following fracture. In dislocation the rupture of the capsule appears to be a fortunate circumstance, for the effused blood can escape from the articular cavity, which blood would be likely to remain for a long time unabsorbed and to furnish a soil for the growth of the bacilli—a process which very probably occurs in many of those cases of tuberculosis following sprains. The tension is thus relieved and absorption more readily takes place.

The majority of cases of bone-and-joint tuberculosis occur in children and in youth. According to Billroth, of all the cases one-half occur before the twentieth year. This is true of certain joints only, for disease of the wrist and of the shoulder is found occurring almost invariably in adults. These joints are more frequently the seat of primary tuberculosis, whereas children are more liable to that form of the disease where the lesion is first found in the bone and subsequently breaks into the joint. These primary nodules often remain in the ends of the bones for a long time without giving any indication of their presence, and Volkmann has appropriately called this the "prodromal stage of joint disease." Hip-joint disease usually begins as a bone disease, and this affection is therefore more commonly seen in childhood. In youth, males appear to be more frequently affected than females, but later in life there does not appear to be any essential difference between the sexes.

It is probable that only a small portion of the tuberculous nodules in joints and bones are primary in origin, the majority of them being secondary to some diseased gland in the bronchial or the mesenteric group, infection taking place through the mucous membrane. Landerer examined post-mortem 150 cases of tuberculosis of the bones and joints, and with one or two exceptions found tuberculous disease of the bronchial glands that evidently antedated the bone affection.

The hereditary tendencies of this disease are shown in the following hospital statistics: According to Brandenburg of Basle, of 141 children with tuberculosis and 162 with bone tuberculosis, all being under four years of age, 34 per cent. were children of distinctly tuberculous parents. Bollinger of Budapest reports 250 cases of bone-and-joint tuberculosis, in 97 of which either the parents or the grandparents were tuberculous.

A considerable amount of experimental work has been performed upon animals to demonstrate the tuberculous nature of the so-called "scrofulous" bone-and-joint diseases. Watson Cheyne was one of the first to perform this work with pure cultures of the bacilli obtained directly from Koch's laboratory. A number of experiments were made upon goats, the nutrient artery of the tibia being injected by entering the tibial artery from below and injecting upward, a ligature having been placed on the vessel above the point of injection. Three minims of the cultures were thus introduced into a young goat, and the animal died on the fifty-second day. In about three weeks from the time of the injection the ankle- and the tarso- and the metatarso-phalangeal joints began to swell, cheesy deposits being found in the lower end of the tibia and the metatarsal bones. The synovial membrane of both joints was swollen and gelatinous. The disease in the joint appeared to be synovial, the epiphyses being but slighly affected.

Krause performed a large number of inoculations upon guinea-pigs and rabbits. The material used was a pure culture of the bacillus suspended in a 0.6 per cent. salt solution. The fluid was introduced either through an incision in the skin, or an injection was made into the peritoneal cavity or into the circulation, as the vein in a rabbit's ear. The culture was also injected into the joint itself. Immediately after the injection the bones were fractured or the joints were bruised and twisted or were dislocated. In the guinea-pigs, out of 44 joints thus treated, 15 became tuberculous, and the joints of 72 rabbits were treated in the same way, of which 29 became infected with tubercle. A microscopical examination of the synovial membrane showed the presence of large numbers of leucocytes in the tubercles, and occasionally epithelioid cells, but no giant-cells. The articular cartilage was rarely affected. The number of bacilli both in the joints and in the bones was in all cases, as in man, exceedingly small, and this was in striking contrast to the great numbers found in tubercle of other organs.

There appeared to be no tendency to the formation of tubercles in the bones and joints when not subjected to trauma. All the cases of fracture healed without the slightest trace of tuberculous infection at the seat of fracture. In this respect the contrast between the action of the bacilli of tuberculosis and that of the pyogenic cocci is very striking, for it is a well-known fact that when an animal is infected with the latter organisms a fracture of the bone will always be followed by suppuration. Tuberculous nodules were occasionally found in the epiphyseal ends of the bones, but not in any large number of cases.

It did not appear that the bacilli were disseminated through the system in emboli, for an embolus was discovered in only a single case. Krause was of the opinion that the bacilli, after being introduced into a vein, were carried through the vessel, and, finally, being taken up by a leucocyte, made the passage through the wall of a vein, or in the bruised tissues passed out at the end of a ruptured capillary vessel into an œdematous tissue or a clot which offered a favorable soil for their growth. The presence of a wedge-shaped infarction of the bone was not observed in any of the cases. W. Muller was able, however, to obtain tubercular infarctions in bone by injecting tuberculous material into the tibial artery of goats. He obtained typical wedge-shaped infarctions. Many of them were, however, round or irregular in shape—a circumstance which coincides with the shape found occasionally in the human subject.

The disease begins as a tubercular ostitis, and its commonest seat is in the centre of the epiphysis or just beneath the articular cartilage. Volkmann remarks that these chronic tuberculous inflammations of bone have a tendency to form in the ends of long bones near the joint, just as pulmonary tuberculosis does in the apex of the lung. On making a section of the bone the tubercular nodule appears as a well-defined mass of a reddish-gray, yellowish-white, or pure yellow color (Fig. 77). The surrounding bony tissue is usually red and hyperæmic, and the trabeculæ may be somewhat thickened. The cancellous spaces are devoid of

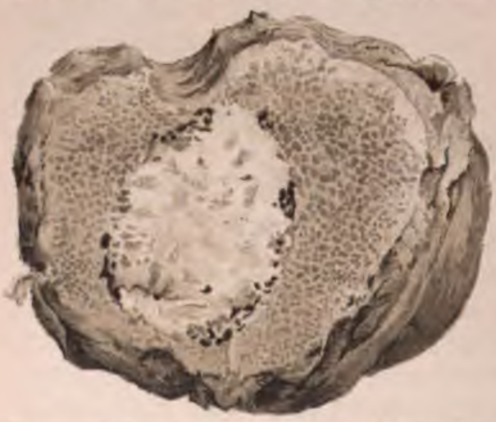

FIG. 77.—Tubercular Nodule of the Head of the Tibia (Sp. 1456–2, Warren Museum).

fat-cells, and they contain a swollen semi-fibrous material. With a magnifying glass the miliary tubercles are seen at the periphery of the nodule, its centre being composed of broken-down cheesy material. The size of these nodules varies greatly. As they grow, the tubercular virus attacks the trabeculæ and leads to their absorption, and the bone becomes softened and breaks up into a mass of greasy, cheesy material containing crumbling fragments of bony tissue. When complete softening has taken place, the material of which the nodule is composed becomes puriform, and it may be washed away, leaving a cavity lined with granulation tissue.

In case the trabeculæ have not completely been destroyed, in the infected part the cancelli between them will become filled with cheesy débris, and as the vitality of the part has been destroyed granulation tissue will form around the diseased mass, and absorption of the connecting trabeculæ occurs: the spongy sequestrum which has thus formed separates from the living bone.

These so-called "cheesy sequestra" are quite small, not exceeding in size that of a walnut, and are more or less globular in form. The surrounding bone may become somewhat thickened, and the interstices are filled with gray fibrous tissue, or eburnation of the bone may in some cases take place (Fig. 78). When the nodule has softened completely into pus the surrounding bone is either covered by a tubercular membrane, which will be described presently, or its surface is infiltrated with granulation tissue, which usually contains miliary tubercles on its inner aspect, affording, nevertheless, protection to the adjacent bone. These small sequestra lie firmly imbedded in a thick layer of blue-gray transparent granulation tissue dotted with yellow spots. Large amounts of pus rarely accumulate around these nodules. When removed and macerated the sequestra are seen to be round or irregularly-shaped bodies, consisting of thickened spongy tissue, and they differ in this respect from the sequestra of osteomyelitis that come from cortical bone, and they are consequently much denser and have usually sharply-serrated edges.


FIG. 78.—Tubercular Abscess-cavity, being the point of origin of disease of the hip-joint (Specimen 1282, Warren Museum).

The sclerosed bone which develops around the diseased area forms, with the granulation tissue, a sort of capsule which may arrest the further progress of the disease, and such sequestra or pus-cavities consequently may remain a long time without giving any sign of their presence. The surrounding bone may, however, eventually be invaded by the tubercular growth, and the thickened trabeculæ may be absorbed, but this rarely occurs.

The tubercles have usually disappeared from the nodule by the time the degenerative changes are well established, and it is with great difficulty that the presence of bacilli can be demonstrated. The difficulty in finding the bacilli is attributed by Cheyne to the fact that they are more numerous in the earliest stage of the disease and decrease later, or they rapidly pass into the spore stage. It is not always possible, he thinks, to stain them. In double staining some are found red and others blue, which result is probably due to the different stages of development.

Very small tubercular nodules may be absorbed, the surrounding bone throwing out granulations that permeate and destroy the broken-down tissues. This action occurs only when the process has not gone on to suppuration, but this rarely happens in children. Some of these nodules are of embolic origin, and in this case an infarction occurs which, terminating in necrosis, leaves a wedge-shaped sequestrum of bone whose base is usually found just beneath the cartilage. These infarctions are found in the articular extremities of the long bones. In its early stages of development the infarction has a gelatinous grayish transparency, and with a lens it will be found studded with submiliary tubercles. It is usually about the size of a bean, but it may occasionally be as large as a pigeon's egg. The amount of suppuration which these sequestra cause is very slight: it may, however, be sufficient to dissect off the cartilage, and then the base of the sequestrum, being exposed to the articular cavity, may become eburnated and polished by friction.

The tuberculous nodules in bone may frequently be multiple. Sometimes both ends of the bone may be involved simultaneously, or separate bones and joints may be affected. There are certain seats of predilection, as the olecranon and acetabulum, the inner condyle, or the neck of the femur, where nodules are more likely to be found than in other bones composing a joint, but these points are not yet well determined by statistics. It rarely happens that the tuberculous nodules give rise to secondary nodules or infiltrations in the surrounding spongy bone. There may be diffused miliary tubercles in a bone as a part of an acute miliary tuberculosis, or in cases where the end of the bone has been freely exposed in the later stages of an aggravated form of tuberculous joint disease.

Where the confluent masses of tubercle in the centre of a nodule begin to break down, there is formed a collection of caseous material surrounded by tuberculous tissue. This material becomes infiltrated with fluids and leucocytes, and thus there is produced a cavity containing fluid fatty material, fragments of cells, and leucocytes, around which there is granulation tissue filled with tubercles; and in this way a tuberculous abscess is formed (Cheyne). It seems, at times, to be quite a matter of accident whether the abscess breaks into the joint or finds its way by a more circuitous route into the surrounding connective tissue. As the tuberculous masses spread, caseation takes place at different points in the wall, and the masses are discharged into the cavity of the abscess; but the spread of the abscess is effected generally by what is termed "burrowing of pus." This burrowing occurs in various directions, and large collections of pus, altogether out of proportion to the original lesion, are formed, and are known as *cold abscesses.* The pus which they contain is so characteristic that it can always readily be recognized after seeing it once. It is of a pale white color, and it frequently contains masses of cheesy material, like coagulated casein, sometimes of considerable size, which makes the aspiration of these abscesses often a difficult operation. It is for this reason called "grumous."[1] It has a very thin serum, much thinner than that of the pus of acute abscesses. Occasionally the pus may be mingled with blood, in which case it will have a dirty brown color. Not infrequently small bony particles are found in the pus, feeling to the finger like grains of sand, particularly in abscesses resulting from disease of the vertebræ. The presence of the bacilli in such pus is not easy to demonstrate microscopically, but on culture the pus of cold abscesses yields a quantity of the characteristic bacilli. The pyogenic cocci are rarely seen in the cold abscess before it is opened: according to many authorities they are never found in them. Rapid rise of temperature and increase of hectic fever accompany the infection of such an abscess by the pus-cocci when an abscess is allowed to break or is opened without the strictest antiseptic precautions.

The walls of such abscesses have a very characteristic appearance, being covered by the so-called *tuberculous membrane,*

[1] From grume, a clot (*grumus,* a little heap; κρῶμαξ, a heap of stones).

described originally by Volkmann. This opaque membrane is several millimetres thick, and is of a violet-gray or a yellowish-brown color, and is very feebly vascular on its inner surface, which comes in contact with the pus. It contains innumerable clusters of miliary tubercles, so that it often appears to be formed exclusively by them. They are supported by a matrix of coagulated fibrin. This membrane can easily be scraped off with the finger or even be removed by a stream of water, and frequently during an operation it peels off from the surface in sheets several inches square. Below this membrane there is found a fibrous indurated tissue which separates the abscess from the surrounding healthy parts. This tissue is the result of a slight reactive inflammation, and it contains no tuberculous material. In over a thousand cases examined carefully by Volkmann, on two occasions only did he see the tubercles invading the surrounding muscular tissue. If on opening an abscess with cheesy contents the muscular tissue is found to have undergone a cheesy degeneration, the abscess is probably syphilitic. In this case no tubercular membrane can be found, and it will not be possible to scrape away the wall of the abscess. The presence of the tubercular membrane is considered by Volkmann as an abso-tutely certain diagnostic sign of the nature of the abscess.

After all the tubercular membrane has carefully been scraped away one can generally find in the subjacent layer of light-colored indurated tissue a small clump of red granulations. These granulations protrude from the mouth of a fistulous opening leading either to diseased bone or to a tuberculous joint. Such a fistulous tract must be followed up to its source, and then there will be found somewhere in the bone a small cavity which gives rise to the more superficial suppuration. Only when this cavity has also been curetted thoroughly can the surgeon feel at all sure that the tuberculous disease has thoroughly been removed.

When the abscess breaks spontaneously it communicates with the surface by an opening, the walls of which are also tuberculous, for whenever the tuberculous pus comes in contact with the healthy tissue infection is bound to occur. Cheyne does not accept the German theory, which assumes that a wall of fibrin has been poured out around the tubercles. He thinks that the granular material of the wall of the tubercular cavity is derived from degeneration of the preformed tissue. Many of these abscesses were at one time supposed to be formed independently of the original nodule or joint disease; consequently they were called "periarticular." Such abscesses occasionally do occur as a result of the transportation of infected material through the lymphatics to an adjacent area of connective tissue, but more careful study of these abscesses, such as has been made since the system of thorough curetting has been established, reveals the presence of the minute fistulous tract which communicates with the original seat of the disease.

As already pointed out by the writer, the tubercular deposit is almost entirely confined to the ends of the long bones, and this pathological fact helps greatly in distinguishing between this form of disease and the necrosis following acute osteomyelitis; occasionally, however, there is seen tuberculosis of the diaphysis or shaft of the long bones. When the disease does occur in this locality, it is found only in quite young children. Such a case the writer saw recently in a boy about four years of age. The presence of a white swelling of the knee-joint of the same limb greatly facilitated the diagnosis. There were a series of sinuses opening at different points along the course of the femoral artery; an exploratory operation disclosed the presence of tuberculous granulations, but no large sequestrum. This condition is somewhat more frequent in the shaft of the tibia, the humerus, and the ulna than in the other long bones, and in these cases it is found to be secondary to some other tubercular focus, as in the case quoted above. Tuberculous deposits are still more common in the shafts of the shorter long bones, such as the phalanges and the metacarpal and metatarsal bones. Miliary tubercles accumulate in the medullary tissue, which is gradually converted into the characteristic granulation tissue; and this tissue, as it grows, absorbs the inner layers of cortical bone and accumulates in considerable quantity. Partly from this accumulation and partly from a deposition of new bone by the periosteum, which is stimulated to a formation of new bone, there is obtained the characteristic flask-shaped bone which was known to ancient writers as *spina ventosa*. This name was given by them to all affections that produced such distention of bone, whether of tuberculous, syphilitic, or other origin: it was suggested partly by the cavities left in the distended bones after the granulation tissue had broken down and melted away, and partly by the appearance of the macerated bones, which appeared to have been distended with air. Gradually the surfaces of the bones yield at the end of weeks or months, and the thinned cortical bone is distended more and more by the growth of the granulation tissue until here and there it entirely disappears. The bones crackle with a parchment-like sensation under the fingers, and fluctuation is finally established at one spot. In the mean time the surrounding skin becomes reddened and swollen, and at some point softens and breaks down, the characteristic tuberculous pus being discharged. These bones may, however, remain for a long time in the granulation stage, and they may eventually heal without suppuration, so that no trace of the disease is left behind. The disease is generally confined to the shaft of the bone, and the neighboring joints may remain perfectly healthy. Although the epiphyses may also escape injury, the intermediate cartilage will probably be destroyed, and the future growth of the bone will consequently be arrested, or the entire shaft of the bone may be absorbed. As the result of the destructive changes great deformity to the fingers or the toes will necessarily result (Fig. 79).


FIG. 79.—Deformity from Absorption of Phalanx due to Tubercular Disease.

Among the short bones is found tuberculous disease of the bones of the carpus and tarsus both in childhood and in adult life. According to Krause, disease of the carpus is not so common in children. At this period of life the disease has less tendency to spread. Whether it be that a bone is affected which does not communicate with the articular cavity or that an adhesive inflammation shuts it off from the other bones, there are often found only a single fistulous opening and a tendency to heal without operative interference. This is particularly true of the carpus. In adults, however, there is a tendency of the disease to spread from one bone to another. The whole wrist is transformed into a spindle-shaped swelling perforated by numerous openings. A sound may be introduced in various directions without detecting a sequestrum. The disease appears to be the expression of a general infection or to be one of numerous local deposits of tubercle, pulmonary tuberculosis being already developed or soon to follow.

In the tarsus a sequestrum is rarely found, except in the os calcis. This region may be infected secondarily to the ankle-joint, or the disease may originate primarily here as a nodule in one or more of the bones. It should not be forgotten that the synovial membrane may be affected primarily as well as the bones. The disease spreads eventually from one bone to another, until the whole tarsus is involved. After long duration of the disease the trabeculæ of the spongy tissue are more or less absorbed by a rarefying ostitis, and the bones become so soft that they can easily be cut with a knife. The whole ankle becomes transformed into a spindle-shaped swelling, from which tuberculous pus is discharged through various openings. The fistulæ and the skin surrounding their mouths are also infected. This disease of the wrist- and the ankle-bones usually receives the name of caries of the carpus and tarsus. By *caries* was meant, originally, an inflammation of the bone, with solution or ulceration of the bone, for bones so affected have, when macerated, the characteristic worm-eaten appearance. The term is falling somewhat into disuse, now that it is known that most cases of caries are, with the exception of the syphilitic forms, due to tubercle. The term "caries" may be applied to tuberculosis of any of the bones or joints.

One of the commonest *seats of tubercular disease*, especially in children, is in the bodies of the vertebræ. Billroth, in a collection of autopsies of nearly two thousand cases of caries of different portions of the skeleton, found that in 35.2 per cent. of the cases the disease was situated in the vertebral column. The disease begins here, as in other bones, where the growth is greatest; that is, near the periosteum and intervertebral substance. It exists, therefore, frequently as a tuberculous periostitis. In this form it is found in the anterior surface of the bone, just beneath the anterior longitudinal ligament. Here the vessels, which run into the bone more or less perpendicularly to the surface, are surrounded with granulation tissue, and the absorption of the bone is therefore greatest at these points; and when the ligament is peeled off from the vertebræ the tuberculous granulations are found adhering to it as small red nodules which have been torn away from the bone, the latter presenting the characteristic worm-eaten look of caries.

Less frequently the centre of the bone is affected, and the tendency to suppuration is then not so great. Two or more foci may exist in the same body. Not unfrequently these nodules contain sequestra. Primary disease of two vertebral bodies in different non-adjacent parts of the spine is rare, though it has been recorded. But no extensive destruction of many of the adjacent vertebræ from primary disease of one may be said to be the rule in Pott's disease (Bradford and Lovett).

The disease may become arrested in its earliest stages, and in this case bone-formation takes place beneath the ligament, and ankylosis of the vertebral column at this point will occur. If the nodule extends between the bodies of the vertebræ, the intervertebral cartilage becomes affected. This generally occurs, indeed, at an early stage of the disease. In rare instances the intervertebral cartilage is affected primarily, and the affection of the bone is secondary (Koenig). As the process advances the bodies of the vertebræ are gradually converted into granulation tissue containing cheesy débris and possibly a sequestrum, and the interarticular cartilage disappears entirely. The bodies of the vertebræ are not only rendered incapable of sustaining the accustomed pressure by the growth of granulation tissue, but they are also much weakened by a rarefying ostitis, which often precedes the spread of the tubercular infiltration. As the disease advances small prevertebral abscesses form, which, as the pus comes in contact with the intervertebral substance, aid in its destruction. The intervertebral cartilage may, however, in rare instances be destroyed by granulations

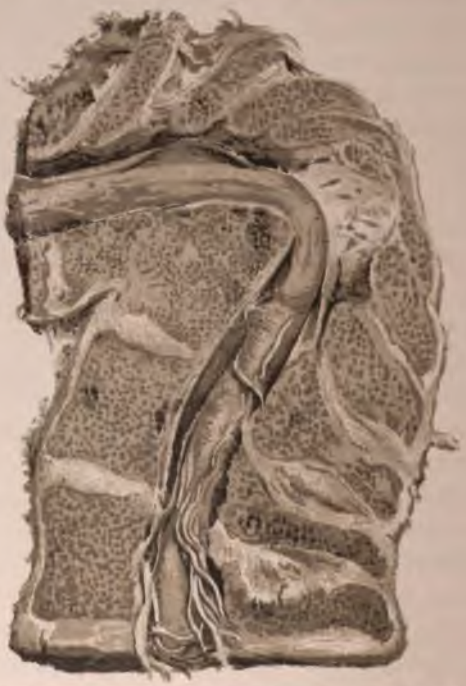

FIG. 80.—Angular Deformity from Pott's Disease. A tubercular nodule may be seen in the arches of the vertebræ (Sp. 1109, Warren Museum).

without suppuration. As the bodies of the vertebræ yield to pressure the characteristic deformity of Pott's disease is produced (Fig. 80). The vertebral body may thus be so nearly destroyed that only a wedge-shaped mass remains to mark the former site of the bone: in this way angular curvature is produced. When several intervertebral cartilages are melted down and the intervening bodies are converted into wedge-shaped masses, the curvature has a more bow-shaped outline. The older writers recognized the fact that the angular curvature indicated disease of but a single vertebral body (Krause).

As suppuration goes on the pus burrows at times for a considerable distance, as in the case of the "psoas abscess," so called, the pus following the sheath of the psoas muscle in working its way to the surface at the groin. Such abscesses originate from tuberculous disease in the dorsal or the upper lumbar vertebræ. Abscesses originating from disease of the lumbar vertebræ may, however, point posteriorly in the lumbar region. Retropharyngeal abscess is caused by disease of the cervical vertebræ. Abscesses arising from the upper dorsal region may involve the pleural cavity, and may even break into the lungs; occasionally the œsophagus and the aorta are bathed in the pus of these abscesses. Such collections of pus may sometimes find their way into the vertebral canal, and spread beneath the meninges and bring about a compression of the cord. The adjacent ostitis may also set up meningitis, and in this case the cord may be compressed by the inflammatory exudation. As a result of this pressure paraplegia may be produced. Pressure of the spinal nerves may occur occasionally as the result of connective-tissue growth around the roots of the nerves. During the period of convalescence ossification of the bones at the seat of the disease may occur as the result of the reparative efforts of the periosteal and osseous tissues, and the fragments of the bodies of the diseased vertebra may thus become firmly ankylosed. The commonest seat of the disease is in the dorsal region; it is found also in the upper lumbar region and, less frequently, in the cervical region. In rare instances the transverse and spinous processes may be the seat of the disease. The flat bones are also the seat of tuberculosis, although much less frequently. In the scapula it may occur with or without formation of a sequestrum; usually there is a carious softening of the part affected. In a case that came under the writer's care the caries affected the greater part of the scapula. By laying open the various sinuses it was possible to curette the bone satisfactorily.

Tuberculosis of the ribs and the sternum is somewhat more frequently seen than that of the scapula. It is usually a disease of adult life. Tuberculosis or "caries of the ribs," as it was formerly called, is either primary or secondary. The latter form occurs after empyema, or other suppurative processes in the thorax, in individuals predisposed to the disease.

The general condition of patients with tuberculosis of the ribs is usually good: in many cases, however, there is marked anæmia, and the prognosis is then unfavorable; but these cases are not common. The disease produces in the bone either periostitis or osteomyelitis. In the latter case a red nodule forms in the centre of the bone, and later the periosteum participates in the inflammation. The trabeculæ and the cortical portion of the bone are absorbed, or if the progress of the disease has been rapid necrosis occurs, and there are found sequestra which, however, are usually not large. Several foci may be established in one rib or several ribs may simultaneously be affected. As the nodules break down suppuration takes place and the pus endeavors to escape in different directions. Usually there forms at the seat of the disease a fluctuating, colorless tumor, on opening which tuberculous pus escapes, and the walls of the cavity are found to be lined with the characteristic tubercular membrane. On scraping this membrane away a small opening will be found communicating with the cavity of the bone. A careful examination will show that the periosteum is thickened and that the shaft of the bone appears to be distended at this point; occasionally the bone is destroyed and a complete solution of continuity takes place, but the formative power of the periosteum usually produces sufficient new bone to preserve the rigidity of the part.

The pus does not point so near the seat of the disease, and it may take a most circuitous route to reach the surface. Riedinger reports a case where an abscess over the rectus abdominis was found to originate from the fifth rib. A fistulous opening over the spinous process of one of the dorsal vertebræ the writer found communicating with a tuberculous cavity of one of the ribs beneath the scapula. This patient eventually died of phthisis. If the periosteum is primarily affected, the disease may spread over a large surface of the rib. In some cases the pus burrows inward, but it rarely breaks through the costal pleura. A pus-cavity of considerable size may, however, occasionally be found projecting into, but completely shut off from, the thorax.

Tuberculosis may also affect the cartilaginous portion of the rib. The disease takes the form of perichondritis, but it may also involve the cartilage, which then undergoes mucous degeneration, and which may be replaced by connective tissue. Tuberculosis of cartilage is an unusually obstinate affection, as parts are involved which lie near vital organs and the reparative power of the cartilage is feeble. The pathological changes in the sternum are very much the same as in the ribs. Owing to the vicinity of the heart and the large vessels, the complications may occasionally prove alarming. The membrana sterni posterior may, however, prove a protection to the mediastinum against the invasion of an abscess.

A case of very extensive tuberculosis of the sternum entered the writer's ward some years ago. The patient was in a cachectic condition. Presently a hæmatoma formed near the site of one of the many fistulous openings, and it soon became evident that a hemorrhage was taking place, from time to time, from a vessel of considerable size. On etherizing the patient, laying open the tumor, and removing the clots, blood spurted from a large artery in the interior of the thorax, possibly the internal mammary. The hemorrhage could only be controlled by plugging the cavity. At the autopsy, a few days later, extensive amyloid disease of the viscera was found. The source of the hemorrhage could not be discovered. The greater portion of the sternum was involved in the disease, and perforation had taken place at several points, but no extensive collection of pus was found in the mediastinum.

Ordinarily, these cases of sternal disease present themselves for treatment with a small fluctuating tumor over the sternum or with a sinus which marks the site of an abscess that has opened and discharged. These abscesses and sinuses, when carefully explored, under ether, are found to communicate with diseased bone. The minute opening leading to the bone-cavity may easily be overlooked, and in some cases is impossible to find, but tubercular abscesses in this locality almost invariably originate from bone disease. The opening of the cavity, as is customary with many surgeons, is not sufficient to effect a cure. Extensive dissection is sometimes needed to expose the tuberculous nodule, and the diseased tissue should be removed thoroughly either by the curette, the chisel, or the trephine, as the case may demand. It is only by such radical treatment as this that a cure can be effected. By the older methods of treatment these sinuses usually lasted for years before healing, or the patient died of pulmonary tuberculosis. In many cases of tuberculosis of the rib a cure cannot be effected without resection of the diseased portion of the bone. The iodoform treatment, which is described in another chapter, is adapted to these cases, but it cannot be depended upon to effect a cure without operative interference.

Among other flat bones that are affected are those of the pelvis.

The most frequent spot is the acetabulum, but the crests of the ilia and the sacro-iliac synchondrosis are also points whence cold abscesses may originate. Tuberculosis of the cranium is found chiefly in the frontal and temporal bone, always excepting the bones of the ear and the mastoid process. A mass of granulation tissue, with possibly a small sequestrum, is found at the site of the disease: in either case a perforation of the inner table and possibly a slight infection of the dura may take place. The disease manifests itself as a fluctuating tumor, which when opened discharges pus and discloses the pulsation of the brain beneath the dura. Syphilis—for which this disease may be mistaken—does not have so great a tendency to form abscesses, and it usually affects a much larger surface of the bone.

That portion of the face most likely to be affected is the infra-orbital ridge. Disease in this locality occurs usually in children, although the writer has seen cases in adults. Suppuration occurs, and ectropion and unsightly scars may be the result of a chronic suppuration lasting for months. A case of tuberculosis of the malar bone caused an extensive suppuration which finally ended in ankylosis of the jaw, for which osteotomy was performed a year after the old sinuses had healed.

Tuberculosis of the bones of the nose is usually secondary to disease of the mucous membrane elsewhere. It may also result from an extension of lupus of the alæ or the septum into the nostril. Isolated patches of lupus are, however, seen in the nasal mucous membrane. It appears as exuberant granulations which at times have a typical papillary growth, or as an ulcer. The cartilaginous portions of the nose are more frequently affected with the lupous type of tuberculosis.

Riedel described large tuberculous tumors growing on the cartilaginous septum in adults, and Koenig saw similar growths in children. Tuberculosis of the nose may also follow tuberculosis of the hard palate, the disease breaking through the floor of the nostril. In a case seen a year or two ago the mucous membrane of the anterior portion of the hard palate and the adjacent alveolar process was in a state of ulceration which had already extended into the nostril. Several members of the patient's family were tuberculous. The diseased portion of the bone was excised and a permanent cure was effected. The lower jaw is very rarely affected by this disease, and the same may be said of the clavicle, although the sterno-clavicular articulation may be the seat of tubercular suppuration.

XXV. SURGICAL TUBERCULOSIS OF JOINTS.

THERE are two forms of tuberculous disease of joints. In the more common (or *osteopathic*) form the disease begins in the epiphyseal ends of the bones, as has already been described. The nodule eventually softens down, and, instead of breaking externally and forming an abscess, it finds its way into the joint, either through a fistulous opening or by gradual involvement of the articular cartilages. In the second variety, the *arthropathic*, the synovial membrane is the seat of the disease.

In the first form there exists a preliminary or prodromal stage of joint disease during which the bone only is affected. The nature of this process, having already been described, need not be repeated here. As the inflammatory process approaches the articular cavity it not infrequently occurs that a reactive inflammation of an entirely non-specific character is set up within the joint. The joint becomes swollen and tender, and it is filled with a serous exudation which may last for some time, and finally disappear (hydrops tuberculosus); or the synovial membrane may become infected and granular without showing any evidence of tubercular infection; or a fine layer of vascular tissue may grow out over the cartilage, closely resembling the pannus growth of the cornea. This tissue may involve the lining membrane of the joint, and it may lead to adhesions and cicatricial contractions to such an extent as to obliterate nearly the whole cavity of the joint. In such an extreme case the severe symptoms of tuberculous inflammation do not make their appearance in the joint, but the tuberculous disease remains confined to the bone. It is often the case with the knee-joint that when the tuberculous nodule which has formed in the bones finally breaks into the joint a greater portion of the inner cavity is shut off by adhesion; consequently the articular surface of but one of the condyles may become affected with the disease. Such an *obliterating synovitis* may occur in the hip-joint, the result of which is that the head of the bone becomes sometimes ankylosed to the acetabulum. Such changes are not unlike those adhesive inflammations seen so frequently in the pleura, the peritoneum, and in other serous cavities, and they seem to protect the joint, to a certain extent, from the tuberculous infection with which it is threatened. This kind of inflammatory reaction is more often seen in the knee than in the hip; consequently suppuration with caries of the articular surfaces is less likely to occur in the knee.

If, however, tuberculous material finds its way into a perfectly healthy joint, it is readily spread about by the movements of the limb into all parts of the synovial capsule, which soon becomes infected: this is well shown by Cheyne's experiments upon animals. Tuberculosis of the joint of a goat was produced by injection of tuberculous sputa directly into the synovial cavity, and also by boring a hole into one of the bones of the joint and introducing the same virus into the cavity thus made. Emulsion of tuberculous pus in distilled water was also injected into a joint with the same result. The same emulsion injected into the femoral artery produced an infarction in the tibia. Pure cultures injected into the knee-joints of rabbits yielded typical results in eleven cases out of twelve.

The infection of the joint from bone occurs by the gradual spread of the tuberculous process through the connective tissue of the Haversian canals, and by gradual absorption of the bony trabeculæ, until finally the tubercular material breaks into the joint by a free opening in the articular surface or by the formation of granulation tissue, which gradually dissects off the articular cartilage. In other cases the deposit may reach the surface at the margin of the synovial membrane, which becomes thickened and shuts off the deposit for a time from the joint-cavity. This thickened patch subsequently becomes infiltrated with tubercles. When an osseous growth of tubercle has broken into a joint we know the disease is at first confined to the synovial membrane, and the tubercular layer can easily be scraped off without sacrificing the ligaments of the joint. Therefore, when the disease has not spread from this point, all that may be necessary is to remove the original nodule or sequestrum and a margin of synovial membrane without resecting the joint.

If the tuberculous nodule communicates freely with the cavity of the joint, the infection of synovial membrane rapidly takes place. The masses of miliary tubercles run together at the point first infected, and thence spread gradually over the synovial membrane, which soon becomes infiltrated with the diseased tissue. In some cases the membrane retains its continuity, the surface is moist and smooth, and is studded with tubercle, which, however, does not have a tendency to disorganize the membrane. When there is an exuberant growth of vascular tissue there may be an extensive formation of granulations, producing the so-called "fungous" type of joint disease.

In still another form there is a tendency to the breaking down of the tubercular masses and to the formation of pus. This type is more frequently seen in elderly people, and the prognosis is usually unfavorable. The membrane is readily perforated, and periarticular abscesses are formed which may or may not communicate with the joint by a fistulous opening. As a result of the entrance of this large quantity of broken-down material into the joint the cartilage and the bones are generally left in a carious condition. Instead of pus there may occasionally be a turbid serum in the joint which may be slightly hemorrhagic. This tuberculous hydrops is, however, not very common.

The *bone type* of joint disease is the commonest form of the two, and it is found chiefly in children, whereas the ordinary synovial tuberculosis is more frequently seen in adults. It seems somewhat to be a matter of chance whether the joint becomes infected with tubercle from the bone, or whether the broken-down products may not find their way to the surface without involving the joint. The cartilage is readily affected by the growth of granulation tissue into the joint, or by the presence of pus, owing to its feeble resisting power. The first change seen is the spread of a fibrous vascular tissue over the surface of the cartilage, the so-called "pannus" growth, which becomes thinner and thinner in passing from the edge of the synovial membrane or from the opening of the tuberculous fistula. Subsequently the cartilage softens, loses its bluish-white color, and changes to a fibro-cartilage, and later to fibrous tissue, which finally becomes infiltrated with tubercle. When the tuberculous material breaks down the softened cartilage may be washed away, and the so-called "ulceration of the cartilage" is produced.

At other times the growth of the tubercular granulations from the subjacent bone is so exuberant that the entire cartilage may be dissected off the head of the bone. This result is occasionally seen in the hip-joint, where the cartilage may be lifted off cap-like.

In the *primary synovial form* of tubercular disease the tuberculous infiltration of the bone is usually comparatively superficial.

A peculiar form of joint disease, described by Volkmann as *caries sicca*, occasionally attacks the shoulder-joint, but it may also be seen in other joints. It is characterized by a growth of scanty, tough, and feebly vascular granulations from the synovial membrane, which growth penetrates the cartilage and gradually eats into and destroys large portions of the head of the bone without the formation of pus. There is often considerable atrophy of the remaining portions of the head and neck of the bone. The usual external signs of tuberculous disease of the bone are of course wanting. It is most frequently seen between the age of puberty and thirty years. It runs its course slowly over a period of one or two years, and terminates in ankylosis of the joint.

Volkmann also described large isolated tubercular nodules (sometimes the size of a pigeon's egg) which project as a pediculated tumor into the joint. The fibrous nodule is composed of dense tissue which contains but few miliary tubercles, or, again, it may contain numbers of tubercles which show a tendency to break down. The adjacent synovial membrane is at first unaffected, but later it is infiltrated with tubercle. Volkmann recommends for these cases extirpation of the nodule with temporary drainage of the joint. A rare form of polypoid growth in the joint is that containing adipose tissue. It may grow to considerable size, and the surface is usually studded with tubercle, which appears to occur secondarily.

In some cases of tuberculous joint disease, particularly those in which there is a sero-fibrinous effusion, rice-bodies are found in large numbers. They appear to consist of coagulated fibrin and of fatty degenerated cells. They are not always associated with tuberculosis, but it is found in certain cases that the synovial membrane is infiltrated with tubercle. In many cases when the rice-bodies are first removed no tubercular disease is found, but the disease may appear later. Their presence in the joint, therefore, is a suspicious circumstance. The exudation of fibrin which occurs with the formation of tubercle seems to be connected in some way with their growth. As in the sheaths of tendons, they may, however, be independent of tubercular disease. They are usually found in joints which have still retained their motion. They may sometimes be felt in the lateral folds of a joint, and their presence may also be recognized by a peculiar crackling sensation like that produced in compressing snow.

The changes in the soft parts connected with the joints are very striking in this disease. The capsules and the surrounding connective tissue, and even certain structures within the joint itself, are transformed into a gelatinous mass. So characteristic is this appearance that it was given the name "gelatinous disease of the joint" by Brodie. Even the muscles and tendons appear to be subject to this peculiar change. In a case the writer remembers seeing the muscular tissue of the entire lower third of the thigh was affected. In some joints the tendons are so matted together by this condition of the tissues that motion of the joint is seriously impaired.

According to Krause, this gelatinous change is not tuberculous in character, but it is due to a venous stasis resulting from the increase in the contents of the joint-capsule and the extra-capsular growth. As the result of the consequent œdema, the mucin, which normally exists in the tissue, is dissolved. A similar development of mucous tissue occurs, according to Köster, in the development of a myxoma. There is found, however, a similar growth of gelatinous material around and in the sheaths of infected tendons when no such obstruction to the circulation exists, and it seems probable, therefore, that the peculiar formation seen so rarely in other forms of disease, and so characteristic of tuberculosis of the joint, must be the result of chemical changes brought about directly by the presence of the bacilli in the surrounding tissues.

The inflammatory reaction may extend from the original nodule to the periosteum, and it may produce an abundant growth of osteophytes which mark the limits of the carious ulceration of the bone. This bony growth is analogous to the callous edges so often seen in chronic ulcerations of the skin in the lower extremities. (Fig. 81).

Fig. 81.—Tuberculosis of the End of the Humerus, showing caries of the articular surface and osteophytes due to inflammation of the periosteum (Sp. 1399, Warren Museum).

Among the numerous pathological changes brought about during the course of the disease are those due to pressure caused by the *spasmodic contraction of the muscles.* This contraction, which is due to reflex irritation of the nerves, furnishes one of the most marked clinical symptoms of the disease. In this way the ulceration of the cartilage is greatly increased, and even the carious bone is absorbed, and the spread of the tubercular process is favored by the pressure. By this muscular action not only great deformities of the spine are brought about, but joints are also dislocated and great deformity is produced.

When the disease takes a favorable turn, cure may be brought about by the absorption of the tubercular tissue and its replacement by healthy granulation tissue. Cicatricial contraction occurs also in the inflamed periarticular tissues. This contraction brings about an impairment of motion which may amount to false ankylosis. In many cases where the anatomical structure of the joint is fairly well preserved there is a diminution in the area of the articular cavity by the formation of adhesions and the obliteration of some of the synovial pouches. When ossification of the cicatricial tissue occurs, true ankylosis results.

In the bones the tuberculous masses—even the sequestra—may be absorbed and be replaced by healthy bony tissue. Cheesy foci, however, may remain for years unabsorbed without showing signs of their presence. These foci are often discovered during operations for correcting deformity. Such a condition shows the possibility of a recurrence of the disease long after the patient is supposed to have been cured. It should be said, however, that these nodules tend to remain local in the majority of cases, and that it is only after an unsuccessful surgical operation that *general miliary tuberculosis* is more likely to result. Disturbances in the normal growth of the bone may be produced by the irregular pressure which is often exerted in a diseased joint. In the so-called "dislocation of the knee-joint backward" the anterior portion of the condyles of the femur may develop more rapidly than the posterior portions. The reduction of such subluxations is prevented by the lateral ligaments, which are insufficiently long to permit the tibia being placed beneath the condyles.

A rare occurrence is an actual elongation of the shaft of the bone, due to chronic inflammatory irritation. *Atrophy* of the bone is much commoner. The fatty tissue in the cancellated spaces of the bone is increased in quantity, the trabeculæ become thinner, and the amount of medullary tissue in the epiphyses and shaft is increased, while the cortical bone is much thinner than usual. Not only is there rarefying ostitis in the interior of the bone, but its dimensions may also be diminished, the bone being shorter and thinner than its fellow. With the return of the natural physiological action the bone regains its normal strength and density, but it will probably never be quite so large as it would have been if atrophy had not occurred before it reached its full growth. If the epiphyseal line is prematurely destroyed, the growth of the bone will be arrested, and then the future use of the limb will seriously be impaired.

Some of the peculiarities of the disease in individual joints may now be studied. In the *hip-joint*, in the greater number of cases, the disease is found originally in the bone, but, according to Cheyne, it does not so extensively occur there as authors are disposed to think. At all events, a large number of cases are examples of primary disease of the synovial membrane. The tubercular deposits more frequently occur in the acetabulum than in the femur. In the latter case they are seen in the head as well as in the neck, and even in the trochanter. The farther they are removed from the joint the less likely are they to involve it. When this cavity becomes affected the disease spreads from the point of reflection of the synovial membrane and from the ligamentum teres over the cartilage. The granulations are filled with miliary tubercles, and they lie on the surface of the synovial membrane or they infiltrate its substance. The fluid in the joint is only slightly increased and altered; it is somewhat turbid and is streaked with pus or with blood. At times the fluid may be distinctly purulent. The ligamentum teres as the disease advances is attacked, and it becomes softened to a pulp. The bone becomes involved first at the edge of the fold of the synovial membrane. The tubercles multiply in the superficial layers of the bone, and they dissect off the cartilage at several points, giving the latter a sieve-like appearance. The same process goes on in the acetabulum, and in well-marked cases of the disease the femoral and acetabular cartilages may lie completely separated between the ends of the bones. Before separation, the cartilage may already have ulcerated in several places, particularly where the head of the bone and the acetabulum press against each other: the effect of this pressure is to increase the amount of ulceration of the bone, and consequently the acetabulum may become enlarged by caries at this portion of its circumference. In the mean time the capsule of the joint is perforated and periarticular abscesses are formed. These abscesses may develop without perforation of the joint, but such abscesses are comparatively rare. In later stages of the disease the tubercular process, after destroying the ligamentum teres, attacks its point of insertion in the acetabulum, and, the bone being gradually eaten away, an accumulation of pus may form within the pelvis. This complication, however, is infrequent. The pus in different cases varies greatly in amount, but in the primary synovial form of the disease it is always certain to be found.

In caries sicca pus is not formed, but this type of the disease rarely attacks the hip-joint.

In the later stages of the disease the joint looks about the same whether it was originally attacked by the synovial or the osseous form of the disease. At this time absorption of the bone has taken place. The head of the femur is partly destroyed by caries, and its bony structure is so softened by rarefying ostitis that when pressed against the acetabulum more or less absorption of the bone occurs. This process is described by Volkmann as "ulcerating decubitus." There is also, from the same cause, an enlargement in the diameter of the acetabulum, due to pressure of the head of the femur after the protecting cartilage has been destroyed. As this pressure occurs with the limb in a state of adduction and flexion, the enlargement of the cavity takes place chiefly in the posterior and upper margins of the acetabulum. This condition is known as the *wandering acetabulum*. As the head of the femur is also greatly atrophied, its displacement from the original portion is therefore considerable, and the resemblance to a dislocation is consequently very close. This displacement in many cases is a cause of shortening of the limb. In other cases the capsule and the ligaments, owing to the distention of the joint by fluid and to the relaxation of the ligaments, are unable to withstand the action of the muscles, and the head of the bone is forced completely out of the socket, or it rests upon the edge of the socket so that a deep groove is worn in its articular surface. The displacements occur very gradually; the relaxed ligaments permit motion in various directions; the joint "wabbles," and a slight accident may therefore result in a sudden dislocation of the bone.

The amount of destruction of bone tissue is sometimes enormous. The head and neck, and even a portion of the shaft, of the femur may be destroyed. In such cases the shortening and displacement of the limb are so great as seriously to impair its usefulness. After the disease has once fully developed there is little probability of a cure without ankylosis, as the structures of the joint have been destroyed before the tubercular virus has been thoroughly eliminated by suppuration. In some of these cases tubercular nodules may remain unabsorbed after the disease is supposed to have been cured. Bradford reports tetanus occurring in a case of cured hip disease, and at the autopsy there was found a large tubercular focus, which was the only source to which the tetanus could be assigned.

In the *knee-joint* at the period of life when the disease is most common—namely, in childhood—the origin of the disease is as frequent in the bone as in the synovial membrane: as age advances the bony form is more common, and the frequency of sequestra in old people makes the disease more obstinate (Cheyne). In old people wedge-shaped sequestra are often seen after injuries. When tubercular nodules are found in the bones the internal condyle of the femur is the point most frequently attacked, but these nodules are often found also in the epiphysis of the tibia.

Tumor albus, or white swelling—which term is applied chiefly to disease in the knee-joint—is due to the formation of granulation tissue in the joint, to the gelatinous change in the tissue about the joint, and to the enlargement of the ends of the bone. The simultaneous atrophy of the muscles of the limb serves to make the swelling more prominent. The whiteness of the skin is due to the absence of all inflammation in the integuments in the early stages of the disease. The development of tumor albus is ascribed by Roser to the frequent use of the knee-joint by a patient who has not yet received treatment. He thinks the thickening of the para-articular tissue is due to the irritation brought about by frequent motion. The minute tuberculous changes which occur in the joint have already been sufficiently described. In no joint can the spread of the tubercular tissue and its destructive effect upon the cartilages be better observed than in the knee. Occasionally the amount of pus formed is considerable, and, as it may not perforate the capsule, it distends the joint, giving a sense of fluctuation like that of hydrops. This condition has been called "cold abscess of the joint." It is not, however, a frequent complication. On opening a joint in well-advanced stages of the disease there is found more disease than might be supposed to exist from the clinical symptoms. The ulceration of the cartilages is well advanced and the synovial membrane is infiltrated with tubercle. Several periarticular abscesses are usually disclosed by the incision, and they may or may not communicate with the joint. It is rare to find a case where there is not considerable disease also of the bone.

In the early stage of the disease there is flexion of the knee-joint from muscular contraction. This flexion brings the head of the tibia in contact with the posterior aspect of the condyles of the femur. The pressure of the bones favors ulcerative decubitus of the cartilage and bone at these points. As the result of the absorption of the bone, which is thus brought about, the head of the tibia slips backward over the femur. This displacement is of course favored by the relaxation of the diseased capsule: it is not caused wholly by muscular contraction, but is due in part to the cicatricial contraction of the diseased and atrophied tissues behind the joint. In addition to flexion there is also a certain amount of external rotation of the leg upon the thigh, which rotation appears to be produced by the position of the contracted limb upon the bed.

The *shoulder-joint* is not a very frequent seat of tuberculosis; when the latter does occur, it is found chiefly in adult life. Primary synovial disease of the shoulder-joint is rare. In fungous tuberculosis of the joint with suppuration there is generally found a primary deposit in the end of the humerus. The greater tuberosity is the most frequent seat of such a nodule, but the head of the bone may also be affected. Disease of the neck of the scapula is uncommon.

The wedge-shaped infarction is a type of the disease not infrequently found in the head of the humerus. These nodules may remain some time without causing suppuration.

Krause reports a case of a man, forty years of age, who suffered from rheumatic pains in the left shoulder. The pain had been so severe that he had been unable for three months to use his shoulder, in the external appearance of which there was little change beyond a slight emaciation. There was, however, marked pain on pressure over the lesser tuberosity. An exploratory incision disclosed a large tuberculous nodule in the head of the bone, which was accordingly resected.

As the disease progresses the localized pain becomes more marked and the patient instinctively holds the arm at rest; the contour of the joint becomes enlarged, and the natural depressions in front and behind the joint disappear. Large cold abscesses may accompany the disease in its later stages. They follow the route of the intermuscular spaces.

The most interesting form of disease of the shoulder-joint is *caries sicca*, which has already been described. The small amount of granulation tissue which develops at any one time and the chronic course of the infection are peculiarities that cause the disease to pass unrecognized. There is great atrophy of the muscular surroundings of the joint, and the head of the bone gradually sinks away and disappears. There is no suppurative inflammation, and, in fact, no sign of inflammatory change. The shoulder is stiff and the arm is held close to the side. The pain is usually severe and radiates down the arm, it being often mistaken for rheumatism. The deltoid prominence disappears and the coracoid process becomes unusually prominent, the condition sometimes closely resembling a dislocation. The writer has seen several of these cases, mostly in young children, and they usually terminate in bony ankylosis.

Tuberculosis of the *elbow-joint* may occur spontaneously or as the result of slight injuries, particularly in children. According to Billroth's statistics, of 1996 cases of caries of the bones, there were 93 cases of disease of the elbow and 239 cases of disease of the knee-joint; in 198 cases the hip, in 150 cases the ankle, in 41 cases the wrist, and in 28 cases the shoulder, were affected. According to Billroth, disease of the elbow holds the fourth place in point of frequency.

The disease more frequently begins in the bone, a favorite spot being the spongy tissue of the olecranon. Volkmann describes such a case where pus was discharged both into the joint and externally. The removal of the sequestrum, with thorough curetting of the bone, was followed by a restoration of the functions of the joint. Nodules may also develop in the epiphysis of the humerus, but they rarely occur in the radius. In certain cases the synovial membrane may first be affected, and the bones will be attacked when the disease spreads to the point of insertion of the membrane in the articular ends of the bone. Suppuration is usually slight. When the bones are affected the presence of the nodule will be indicated by localized pain and by some enlargement of the bone. If the synovial membrane is first attacked, an elastic swelling usually shows itself between the head of the radius and the olecranon. The movements of the joint are impaired early, as indicated by inability to extend fully the arm.

As the joint gradually becomes disorganized the surrounding tissues are swollen, and they undergo the characteristic gelatinous changes, and in extreme cases there is a well-marked tumor albus with the spindle-shaped swelling. As pus forms numerous sinuses open, and the tuberculosis may eventually extend even to the skin. In old persons and in those who have been treated unsuccessfully by some operative procedure the disease of the soft parts may become very extensive, necessitating amputation.

The *prognosis* in tubercular disease of the elbow is not favorable for the re-establishment of motion unless the affection is treated at a very early stage. This joint is so complicated that the disease involves a large and a comparatively widespread surface of synovial membrane before its presence is discovered (Bradford).

In studying the *clinical symptoms* the point of origin in the bones must be sought for chiefly in the early stages of the disease. The period during which the morbid process remains confined to the bone is often a long one. In some rare cases several years may elapse before the disease advances beyond this stage. It will readily be seen that the beginning of the affection is very gradual and insidious. The patient experiences an inability to use the joint, and there is some slight stiffness. If one of the joints of the lower extremity is affected, there will be slight lameness. If it is a superficial joint, such as the knee- or the elbow-joint, there may be slight swelling of some portion of the bone, pressure upon which gives rise to pain. As these nodules enlarge pus may form and a fragment of the bone with pus may be discharged. The adjacent joint may at this time suffer from non-tubercular synovitis due to its proximity to the tubercular inflammation. As the result of such changes there is an enlargement of the joint. The anatomical outlines disappear and the joint may assume a more or less spindle shape. The veins are more or less injected, and the skin becomes somewhat thin and shiny like the top of a bald head (Krause). The enlargement of the joint is emphasized by atrophy of the muscle. In tumor albus of the knee the muscles of the thigh and the calf are affected in this way. The adipose tissue is largely absorbed, and even the skin in some cases seems thinner than normal. Measurements of the limb will show a diminution in its circumference at an early stage. In the later stages of the disease the muscle may undergo degeneration and absorption of the contractile substance.

Muscular fixation is a symptom of nearly all forms of tubercular joint disease. The joint is usually flexed or adducted, and is more or less rigidly held in that position. This abnormal position of the joint has been attributed to distention with fluids, it being supposed that the flexed position gives the most room for fluid; but the flexion is undoubtedly due to muscular spasm from reflex irritation. In hip disease spasm is one of the earliest symptoms, and it has been said that there can be no disease present if there is no limitation in the motion of the joint. When the joint is more or less disorganized this contraction of the muscles may lead, as has been seen, to subluxation.

Pain is a prominent symptom of joint disease, although occasionally it may entirely be wanting. Reference has already been made to rheumatic pains accompanying caries sicca in the shoulder-joint, there being frequently a painful point anterior and external to the coracoid process. In hip disease the pain is almost invariably situated in the knee, and there is great sensitiveness to jarring of the limb. There is an unconscious protection of the joint in the movements of the patient. The reference of pain to the knee is attributed by Bradford and others to the intimate relations and anastomoses of the sciatic, obturator, and anterior crural nerves. According to Sayre, the pain is the result of the struggle between the adductor muscles and the distended capsule. The so-called "night-cries" which occur in the early stages of hip disease, and more rarely in knee-joint disease, are described by patients as caused by an extremely sharp and severe pain suddenly interrupting sleep, and leaving an ill-defined sense of aching in the thigh and hip as if the hip had sustained a blow.

The next important point of tenderness on pressure lies in the groin just external to the femoral vessels. Tenderness is detected in the knee on the inner surface of the head of the tibia. Pain is not, however, severe in the knee except in acute exacerbations. The anterior and lateral portions of the ankle-joint are the tenderest spots. Pain on pressure is felt at the elbow-joint over the head of the radius and the neighboring part of the capsule. Pain in Pott's disease is generally referred to the back of the head, the shoulders, the chest, and the abdomen. In the latter case the child usually complains of "stomach-ache." Tenderness on pressure over the spine is not a symptom of this disease.

Heat is a symptom that can be relied upon in certain stages of disease or in certain joints. In the knee when the disease is well developed heat is usually present, especially if any exacerbation takes place.

There is usually little if any febrile disturbance during the early stages of the disease and while it is confined to the bone or joint. Even when a cold abscess is present the rise of temperature is only slight, varying from 1 to 2° F. Fever may occur, however, if pulmonary tuberculosis supervenes or if there is tuberculosis of the intestinal canal or basilar meningitis. In cases of miliary tuberculosis there may be considerable fever, and it may be of the continued type. There is great exacerbation of both local and constitutional symptoms when a cold abscess breaks. The joint swells, the skin is reddened, and the discharge assumes the character of a phlegmonous suppuration. There is high fever, and generally there is increased emaciation. These changes are due to a mixed infection with pyogenic cocci. Eventually this fever is of the hectic type, consisting of an evening rise of temperature, with a return to the normal in the morning. Pronounced anæmia is regarded by some as an unfavorable symptom in different forms of tuberculosis, as it is an indication that generalization of the tuberculous virus has taken place.

Cure may take place spontaneously even in most aggravated cases, but generally with ankylosis or deformity. Even abscesses of considerable size may be absorbed.

A fair amount of motion often remains in some joints after recovery, a portion only of the joint having been destroyed by the disease. It is not uncommon for relapses to occur several years after apparent cure has taken place, the new infection being derived from the cheesy material remaining imprisoned in the cicatricial tissue. In unfavorable cases there is apt to be found albuminuria, which is usually caused by the presence of amyloid degeneration of the kidneys. These changes are probably brought about by chemical substances which are taken up into the lymphatic system, and occasionally the lymphatic glands are seen thus affected. Although the statement is made that such degeneration permanently destroys the function of tissues or the organs thus affected, it is possible that after cure of the joint has taken place the amyloid degeneration may disappear. In a case of tuberculosis of the neck and trochanter of the femur of several years' duration, followed by purulent synovitis of the knee-joint, there was evidence of an amyloid degeneration of the kidneys and spleen and some enlargement of the liver, the signs of which degeneration disappeared after a successful amputation of the hip-joint. Pulmonary tuberculosis may occur as a complication, particularly in connection with caries of the carpus. Children are more likely to be affected with miliary tuberculosis in unfavorable cases, especially after operations have been performed.

From what has been said about the pathology of tuberculosis of bones and joints it will be gathered that all the affections hitherto known as caries of the joints, scrofulous disease, gelatinous disease, fungous or strumous affections, spina ventosa, etc. are, almost without exception, forms of tuberculosis. As the cachectic condition marked by anæmia, emaciation, and hectic fever does not develop until the later stages of the disease, the student must not be led into supposing that a good general condition of the patient precludes the *diagnosis* of tubercular disease; for a nodule may remain for a long time concealed in the cancellated tissue of the bone without producing any constitutional disturbance whatever. There are a number of other forms of infectious bone disease, which, however, begin, as a rule, as acute infections, and which subsequently become chronic. The most frequent of these infections is acute *osteomyelitis*, which may often lead to suppuration of the joint and to destruction of the articular cartilage. This affection begins as a very acute inflammation of the bone, and frequently with profound constitutional disturbance. After necrosis has taken place and the abscess has broken and fistulous openings have formed, the acute stage passes away and the patient is left with chronic suppuration of the bone. This condition is, however, readily distinguished from tuberculosis, as the inflammation involves the shaft of the bone instead of the epiphysis. The previous history of the case and the presence in the shaft of a large sequestrum which has the shape of the original bone will enable one to make the diagnosis of osteomyelitis in most cases. The appearance of the fistulous openings will also be a guide, for in this form of bone disease the tubercular granulations are absent. In those rarer forms of osteomyelitis found in the epiphyses of the bones the difficulty of diagnosis is greater. An effort should be made in such cases to demonstrate the presence of tubercle bacilli, although their absence will not definitely settle the point, as they are difficult to find even in well-marked types of osseous tuberculosis. The tubercular sequestra are, as a rule, smaller and more irregular and are filled with cheesy material. Many forms of *syphilis* of the bones are not readily distinguished from tuberculous disease. There is not the same tendency to suppuration in syphilis, and the disease usually affects certain localities. Syphilitic caries of the bones of the cranium is usually very extensive, and it often runs its course without suppuration. It is so typical a form of the disease that when once seen it is not likely to be mistaken for anything else. There is sometimes a tendency to the formation of sequestra. The writer has seen extensive disease of this kind in the frontal bone, but in such cases the history points so distinctly to a syphilitic origin that a mistake in diagnosis is not likely to be made. When suppuration does take place the pyogenic membrane is tough, and it cannot be scraped off the subjacent tissue, whereas in tuberculosis the membrane is removed with great ease. A syphilitic gumma may sometimes form in the capsule, and may closely resemble an isolated tubercular nodule. These cases will of course yield to treatment with iodide of potassium.

Metastatic inflammations of the joints occasionally occur as complications of acute exanthemata, a portion of which inflammations are the result of septic or pyæmic infection, and a certain number of them are cases of tuberculous infection which has developed during the favorable conditions offered by the diseased state of the system. Volkmann suggests that some of them may be due to the action of the virus of the exanthema.

Serous effusion into the knee-joint, *hydrops articuli*, or "water on the knee," occasionally assumes a type which may suggest the possibility of tuberculosis. There is, in such cases, a so-called "arthritic atrophy" of the muscles, with impairment of the nutrition of the limb that is suggestive of organic disease. A careful examination, however, will clearly show the true state of affairs. The "fluctuation" of the patella, the absence of pain on pressure or of grating of the joint or of any infiltration of the soft parts, are sufficiently characteristic symptoms of this affection. *Neuralgic* or *hysterical joints* often disable persons who have sustained a slight injury, and they cause much anxiety. An examination in these cases shows an absence of all pathological changes. The shifting character of the pain and the presence of nervous or hysterical symptoms will aid in the diagnosis. Such symptoms yield readily to massage.

Arthritis deformans occurs chiefly in elderly people. The characteristic changes in the bone are so pronounced that a mistake in diagnosis is not likely to be made. The changes in the soft parts are much less marked than in tuberculosis.

Periosteal sarcoma may sometimes be mistaken for tubercular disease. The writer has opened a supposed tuberculous knee-joint to find sarcoma of the femur. Myeloid sarcomata are usually found in well-recognized spots, such as the head of the tibia, or more rarely in the condyles of the femur and in the carpal extremity of the radius.

In the advanced stage of tuberculosis the disorganization of the cartilages or the capsule enables one to obtain crepitus by free lateral rubbing of the articular surfaces against one another. Even when crepitus cannot be obtained the abnormal mobility of the joint is a suggestive symptom.

The *prognosis* of these diseases is far more favorable in children than in adults, and in estimating the value of any special mode of treatment it is important to bear this fact in mind. It should not be forgotten also that the severest types of bone-and-joint disease may heal spontaneously, as the conditions for limiting and subsequently for absorbing the tuberculous foci are more favorable in bone than in the internal organs; as, for instance, the lungs. In the former case the disease is shut in at first by a dense wall of bone or by the tough envelope of a joint capsule; in the latter case the infective products of the disease spread over the mucous membranes for a long distance before they are expelled, and in this way the disease is readily generalized. This localization is more marked in children. A diffuse suppuration of the carpus or of the tarsus is rare at this period of life, and a minor operation usually suffices for the cure of the affection. Caries of the wrist in adults is almost always followed by pulmonary tuberculosis. Resection of the ankle-joint for the disease in adult life is generally considered a useless operation, and amputation is practically the only resource in tuberculosis of the carpus and tarsus at this age.

The statistics of this disease do not show a very large percentage of cures. Billroth estimates the mortality of cases observed by him during a period of sixteen years to be 27 per cent.; Koenig records a mortality of 16 per cent. in 177 operations extending over a period of four years. Even if a local tuberculosis is successfully removed, it does not prevent the possibility of a later infection of the lungs or other organs, as the susceptibility of the individual still exists. It will remove, however, the danger of miliary tuberculosis starting from this point. A local return shows that the operation has not thoroughly been performed.

It is important to remember that even when the original focus has been removed the secondary abscesses and sinuses, if allowed to remain, are equally a great source of danger. In adults these secondary complications are even more dangerous than the original affection.

The difference in the prognosis in the diseases of different joints is very great. The destructive processes which proceed in the hip-joint are more extensive and are more likely to be followed by suppuration than those that take place in the knee, where a tendency to cicatrization often sets in early. In the most favorable cases it is unsafe to promise a cure in less than two or three years, and it should be borne in mind that there is always danger of a relapse even after several years of health.

The *constitutional treatment* of tuberculous disease of the bones and joints differs little from that employed for other forms of tuberculous disease. The great majority of the patients afflicted with this form of tuberculosis are unable to avail themselves fully of one important feature of the treatment, which consists in the selection of a suitable climate or of suitable surroundings. In European countries great importance is attached to a sea climate, many of the largest cities being situated in the interior of the continent. The important point to be obtained in most cases is a liberal supply of healthful air. A country life is therefore, as a rule, most favorable for a tuberculous patient, particularly a child, if the patient is not thereby deprived of too many home comforts. A liberal supply of fresh milk and eggs is one of the principal points to be insisted upon in the diet. Among drugs cod-liver oil takes the first rank; the refined preparations of to-day have deprived this drug of many of its obnoxious qualities. It is well to advise the pure oil, to be obtained from as reliable a source as possible, and to enjoin the greatest care and cleanliness in the preservation of the bottle and cork and of every article used in its administration. In this way it may be administered in moderate doses for a long time without disturbing the digestion: one to two drachms for a child and three for an adult are usually sufficiently large doses. Preparations of phosphate of lime are supposed to favor bone-repair. Whether this supposition be true or not, they serve as exceedingly valuable tonics in this disease. The syrup of the lactophosphate of lime may be administered in teaspoonful doses to children, and it is a preparation which they all like. The compound syrup of the hypophosphites, containing potassium, sodium, iron, manganese, quinine, and nux vomica, is equally useful for adults: it may also be given in drachm doses. Preparations of iron are indicated when in the more advanced stages anæmia begins to make its appearance, the syrup of the iodide of iron being considered one of the best. When amyloid degeneration of the kidneys and albuminuria make their appearance the administration of iodide of potassium internally is said to be of great benefit, the amount of albumin diminishing markedly during the use of the drug (Krause).

One of the earliest forms of *local treatment* to be applied to a joint is fixation, which should be employed during the acute stage when the tubercular process is exciting surrounding inflammatory reaction. In this way inflammation is not aggravated, and many of its symptoms, such as pain and swelling, are immediately relieved. This alleviation can be accomplished in most joints by the use of the stiff bandage, which also possesses the great advantage of exerting gentle and continuous compression. Compression is a most effective agent in producing absorption, and it is particularly valuable during the granulating stage of the disease and before suppuration is established. The use of the stiff bandage on the knee-joint may sometimes be continued through a series of years with the most satisfactory results. At first a thin layer of plaster of Paris may be used, with a coating of silicate of potash or of dextrin. But later in the treatment a light dextrin or a silicate bandage may be applied and be renewed two or three times a year, and in this way the compression can be kept up over a long period of time. This treatment is more applicable to the knee than any other joint, but it is employed also in disease of the hip, the ankle, and the wrist, and more rarely in disease in the elbow; in the shoulder-joint it can be of little use. The advantages of the plaster jacket in Pott's disease are great, and its cheapness makes it a useful substitute for apparatus when expense is a matter to be considered.

Another important element in the treatment of joint disease is extension, which is employed to overcome the spasmodic action of the muscles by which the pressure of the inflamed bones upon one another is increased. This increase of pressure not only favors the spread of the tuberculous disease, but produces in many cases also, as has already been seen, an absorption of the bone (ulcerative decubitus), which adds greatly to the deformity. Extension at one time was supposed to separate the diseased bones, but experiment has shown that the actual separation that occurs is but slight and under conditions which do not exist clinically. This mode of treatment is more applicable to the hip and knee than to any other joints, and it prevents or corrects flexion or abduction or subluxation, besides relieving many of the symptoms of inflammation. Those forms of extension apparatus which oblige the patient to lie in bed are suitable only when the symptoms partake of an acute type, but for the more chronic forms the traction splints, such as have been devised by Sayre and Taylor, are to be preferred, as they permit locomotion. In the later stages of the disease, particularly of the hip and knee, traction may be replaced by protection. Protection is obtained by the use of crutches and by a high sole on the opposite foot, so that the diseased limb may swing clear of the ground during locomotion, or by means of the so-called "perineal crutch," an apparatus which may be worn beneath the clothing for the support of the limb. The support should be continued for a considerable space of time after all active symptoms have disappeared.

The malposition occurring in the knee-joint must be overcome by extension or by forcible reduction by flexion. If the joint does not yield to extension by weight-and-pulley in bed, the patient should be etherized and sufficient force be exerted to straighten the limb. Occasionally there will have been so much muscular contraction that many of the tendons near the popliteal space must be divided before the limb can be straightened. After straightening has been accomplished it is advisable to keep the limb in a stiff bandage or in some form of apparatus to prevent a return of the deformity. Bony ankylosis in an unfavorable position can be relieved only by osteotomy. Malposition from ankylosis occurs occasionally in hip disease, but an excellent result may be obtained by cutting the femur just below the trochanters or through the neck, thus making it possible to straighten the limb.

In the knee-joint the patella is occasionally ankylosed to the femur. If the patella offers an obstacle to the correction of a deformity, it may be separated from its attachment to the bone by the chisel.

The *treatment of cold abscess* has varied greatly during recent years. When the antiseptic treatment was introduced, some of its most beneficial effects were supposed to be illustrated in the treatment of this affection. Although septic infection with pyogenic bacteria was thus prevented, no effect was produced on the tubercular process, and the abscess was simply converted into a tubercular sinus. A great step in advance was made when the tubercular nature of the pyogenic membrane was recognized. The method was then adopted of scraping away the membrane after laying open the abscess by a free incision. But the difficulty remained of not always being able to reach all the folds of the abscess-cavity, and small sinuses leading to concealed foci of disease were often overlooked; consequently the source of the whole trouble would remain untreated. The healing properties of *iodoform* in the treatment of tubercle having long been recognized, a method was finally devised whereby this drug could be brought in contact with all the ramifications of such a pus-cavity. Among the first to introduce this method were Billroth and Mikulicz. The following is Krause's description of the method:

The abscess is first tapped under antiseptic precautions. It is best to use a good-sized trocar, so that clots of cheesy material and fragments of abscess-membrane can be removed readily through it. The cavity is then thoroughly irrigated with a 3 per cent. solution of boracic acid, and the iodoform preparation is injected. Solutions of iodoform in ether or in alcohol are more readily absorbed, but they may cause poisoning, and they have the disadvantage of leaving but a small quantity of the iodoform in the cavity. Krause objects also to iodoform oil on the same grounds. He uses a 10 per cent. solution—or, rather, suspension—of iodoform in glycerin. Another preparation is a 10 per cent. suspension of iodoform in water with 20 per cent. glycerin, 5 per cent. gum-arabic, and 1 per cent. carbolic acid. The finely-powdered iodoform is rubbed up with a few drops of glycerin, and is gradually added to the mixture, which must be well shaken before using. When properly prepared it can easily be injected with a hypodermic needle. As this drug is only in suspension, it is not absorbed, and it remains in contact with the pyogenic membrane. A gradual absorption does of course take place, but not with sufficient rapidity to cause poisoning. It is well to act with caution in cachectic subjects. For adults about 3 ounces of such a mixture may be introduced. Smaller doses are, however, more frequently used. The abscess-walls should be so manipulated as to bring the mixture in contact with all the folds of the membrane. It is not usually necessary to put a stitch in the puncture wound, a light dressing being all that is needed. If the trocar is plugged with cheesy clots, an incision may be necessary, which must of course be sewed up before the injection is made.

After the first injection the swelling subsides, and in some cases it disappears entirely in a few weeks. Two or three injections are, however, usually necessary at intervals of a few weeks. If the abscess refills, it must be washed out again with boracic acid. In this case several months may elapse before a cure is effected. At the second puncture the discharge through the canula is of a more mucous character and of a darker color, and it is mixed with particles of iodoform powder. Later the fluid becomes clear and ropy, containing under the microscope round cells in a state of fatty degeneration. Occasionally a fistula forms which discharges a similar fluid, sometimes in considerable quantity, but the healing process does not appear to be disturbed.

Iodoform appears to cause a breaking down of the tuberculous tissue, which is then thrown off. If fragments of the wall of such abscesses are examined microscopically from time to time, it will be found that the bacilli have disappeared soon after the beginning of the treatment. The tubercles are seen infiltrated with round cells and serous exudation, and many of the cells of the tubercle are in a state of fatty degeneration. The subjacent fibrous layer throws out granulations which destroy and throw off the tubercular membrane. When all the broken-down material has disappeared the granulations cicatrize and the abscess heals.

In tuberculous joints the same treatment may be carried out. If there is pus in the joint, the treatment is the same as for abscess, a smaller quantity of the mixture being used: about an ounce is sufficient. A trocar about 2 mm. in diameter is better than a hypodermic needle. Passive motion may be employed to spread the mixture through the joint. It has no bad effect upon healthy cartilage.

In the wrist the best point to select for puncture is just below the styloid process of the radius and ulna. In the elbow-joint the head of the radius is considered the most available spot. In the shoulder-joint the trocar may be introduced externally to the coracoid process, just outside the spot where the spine of the scapula becomes continuous with the acromion. In injecting the hip-joint a long trocar should be used; the limb should be extended, slightly adducted, and rotated inwardly. The instrument, which is inserted just above the trochanter major, should be pushed until it comes in contact with the head of the bone. In tapping the knee-joint care must be taken to insert the instrument beneath the patella. In the ankle-joint the point to enter is under the tip of either malleolus. Anæsthesia is usually unnecessary, but a 1 or a 2 per cent. solution of cocaine may be used for the skin. A slight rise of temperature occurs for one or two days after the injection, but it is of no pathological significance. Three injections performed at intervals of about four weeks are usually necessary. There is considerable relief of pain after the first injection, but the swelling does not subside with rapidity. The tissues become, however, somewhat firmer in favorable cases. If there is pus in the joint, it generally returns after the first injection, but after the third or fourth injection it disappears. The restoration of motion to the joint will depend upon the amount of change which has already taken place, but cases of complete return of the normal movements are reported.

This mode of treatment appears best suited to young people and children, though adult life does not constitute a contraindication. The treatment is well adapted to tuberculous wrists, even when pulmonary disease is present. The method should be tried even in severe cases before resorting to operation. It may be tried in cases of primary epiphyseal disease as well as in tuberculosis of the synovial membrane. It should always be employed in cases of suppurating bone disease so situated that the bone cannot easily be reached by the operator. If, however, the bone can readily be reached through the abscess, an operation is to be preferred, for in this way the surgeon is in a position to leave the parts in a condition favorable for permanent cure. Balsam of Peru has largely been used in the same way, but not with such brilliant results.

Billroth lately adopted a combination of the old method of scraping an abscess and the iodoform-glycerin treatment. The abscess is first laid open by a long incision, and the lining membrane is thoroughly scrubbed off with iodoform gauze or some similar material, and, after the bleeding has been stopped, fistulous openings are sought for and traced to their source, counter-openings being made, if necessary, for the purpose. The primary nodule, being found, is then thoroughly curetted away. The whole cavity is now washed out with 1 : 3000 corrosive sublimate and is stuffed with iodoform gauze. The Esmarch bandage, if applied, is then removed. The gauze is left in for one-half to three-quarters of an hour or until the next day, and is removed after being wet with a sublimate douche: the surface is dried, and the wound is sewed up with a sterilized continued suture under the most careful antiseptic precautions. An opening of some size is left through which the iodoform-glycerin is injected. If the glycerin does not flow well, it must be forced through a tube into all parts of the cavity, which should be filled sufficiently to expose the inner wall to the fluid without over-distention. The stitches should not be drawn too tightly, because they prevent healing by first intention. Finally, the wound is entirely closed and a dressing with gentle compression is applied. Those parts of the body where compression cannot easily be applied are not suited to this method, as slight hemorrhages from the walls of the cavity are apt to take place.

Usually there are three or four days of fever with a high evening temperature. The dressing is allowed to remain, if all goes well, for two or three weeks. In other cases the fever and pain are so great that the dressings have to be removed, and the emulsion, mingled with blood, will be found oozing up between the stitches. In this case the emulsion must be pressed out and drains be inserted between the stitches, or the wound may be opened slightly and the blood be pressed out, and healing without suppuration may still occur. Billroth adopts this treatment also to open abscesses. Iodoform-poisoning is rarely seen.

A 10 per cent. emulsion of iodoform in olive oil, or equal parts of iodoform and olive oil, may be used in many cases: such treatment is well adapted to open sinuses, and can safely be carried out by the patient himself. It is of course not so effective as one applied before the abscess is opened, but it gradually brings about an improvement in cases not amenable to treatment in any other other way, and it is useful in healing a sinus that may have remained after operation, or it is adapted to the preliminary treatment of open sinuses before attempting operative interference. In fact, the iodoform treatment is a valuable preliminary treatment to any operation that is intended, and the success which it has thus far met with, and the ease with which it can be carried out, even by those who have not the conveniences of a large clinic, recommend it strongly for general trial.

In dropsical forms of tuberculosis of the joints (hydrops tuberculosus) the effusion may be treated by the method sometimes employed for non-tuberculous dropsy of the joint. This method consists in the introduction of a canula, and, after drawing off the fluid, injecting a solution of carbolic acid of the strength of 1 : 60. After manipulating the joint so that the fluid shall come in contact with the entire synovial surface the solution is drawn off and the puncture is covered with an antiseptic dressing. Great care must always be taken to procure strict asepsis during such an operation.

There are a large number of cases of bone or joint disease which are not relieved by any of the methods of treatment hitherto mentioned. Formerly all these cases eventually came to excision or to amputation, but the present knowledge of the pathology of these affections, and the extent to which the different parts of the joints are involved in different cases, and the great security and precision offered by bloodless and antiseptic modes of operating, enable one to choose from a much greater variety of operative procedures.

Resection of the joint will obviously be unnecessary where a *tuberculous nodule* exists in one of the epiphyses which it is desired to remove. It may be sought for and readily be found if a fistulous tract is present; otherwise an exploratory incision must be made for the purpose. A flap of skin with the periosteum may be reflected from the bone, and an exploratory puncture may be made with the chisel in several places until the nodule is discovered. In removing the disease care should be taken, if suppuration or cheesy degeneration has not already occurred, to cut into the healthy bone, and to avoid, if possible, bringing the diseased mass in contact with the healthy tissues. If the nodule has softened and broken down, the cavity must be scraped out thoroughly with a curette, and if there is a sequestrum present it must be pried out with an elevator. The walls may, if necessary, be chiselled down to healthy bone even at the risk of making an opening in the joint. The cavity thus made can then be disinfected with a solution of 1 : 1000 corrosive sublimate, or, if it is doubtful whether all disease has been removed, it may be seared by the actual cautery. Some operators, relying upon the thoroughness of their operation, allow the space to fill with blood-clot after removing the Esmarch bandage, and then seek to obtain union by first intention; but there is always danger that a local return may thus be facilitated, for if there be any of the infectious material left behind, the blood-clot offers a most favorable soil for its development. It is better, therefore, to fill the cavity with iodoform gauze and allow it to heal by granulation. Senn suggests the introduction into such cavities of fragments of decalcified bone that have been covered with iodoform. These fragments offer a suitable scaffolding for the development of the granulations, and at the same time the iodoform diminishes the danger of local or of general tubercular infection. The danger of general infection must always be borne in mind whatever operation is being performed, for acute miliary tuberculosis may result from an infection of the surrounding healthy tissues of an operative wound.

Tubercular nodules in parts of the skeleton remote from joints may be treated in the same way. A portion of the rib may be resected if necessary, or the surface of a flat bone may be trephined or chiselled until all diseased bone has been removed.

When the diseased nodule or sequestrum projects into the joint, it may be necessary to open the joint to facilitate its removal. The operation to be performed in this case is *arthrotomy*. A number of such operations have been successfully performed. Arthrotomy consists in making an incision into a joint for the removal of a foreign or diseased body. It may be in the form of a large transverse cut which lays the joint open freely for inspection, or it may be a simple linear incision, or, finally, a flap of integument and perhaps of periosteum may be reflected for the purpose of exposing the seat of the disease. After removing the diseased bone, and, if need be, curetting some adjacent infected portion of the joint and dusting with iodoform powder, the wound is closed and a small drain or tent of iodoform gauze is allowed to remain between the lips of the wound. After any such operation in or near a joint the limb should be placed upon a splint, so as to secure complete fixation during the early stages of the healing process. Such nodules are found in the anterior or in the lateral portions of the epiphysis of the tibia, in a condyle of the femur, in the neck or the trochanters of the femur, and in the olecranon process of the ulna; in nearly all of which cases it is not impossible to make an opening into the diseased cavity without involving the joint. Several cases of exploratory incision into joints have resulted in their cure, very much as in laparotomy for tubercular peritonitis.

In deciding upon some of the more serious forms of operation it should be remembered that the functional results after excision of the joint are inferior to those obtained by conservative treatment. Moreover, any operation which involves the epiphyseal line interferes seriously with the growth of bone. Although in tumor albus there may be an arrest of the growth of bone, the shortening after an extensive incision, as of the knee-joint, is far greater than after a spontaneous cure (Bradford).

These operations should therefore be attempted only when, in children, considerable collections of pus are found in the joint and more or less profound constitutional disturbance exists, as shown by the presence of fever and weakness and loss of appetite. Considerable displacement of the bones also indicates an advanced stage of the disease. In adults, after a trial has been made of the various forms of conservative treatment, it is better to adopt a mode of treatment that will lead to rapid healing, rather than to run the risk of pulmonary tuberculosis or amyloid degeneration of the internal organs. The advent of suppuration with the formation of an abscess communicating with the joint that cannot be controlled by the usual treatment is apt to be followed by the establishment of fistulous openings of a tuberculous character and a hectic fever. Under these circumstances it would be unwise to postpone too long resection of the joint. The presence of a dislocation or subluxation in the hip must be an indication for resection. In the knee a subluxation could probably be remedied by other means unless extreme in degree.

The patient's station in life will influence the surgeon somewhat in the selection of a mode of treatment. In a laboring man an operation leading to a cure in a few weeks' time may be selected in preference to a more conservative treatment, although the latter might be successful in the course of two or three years.

Arthrectomy is an operation designed, as its name implies, for the removal of the structures forming the inner surface of the articular cavity. In its narrow sense it is limited to an excision of the synovial membrane, cartilage, or bone. The latter operation has sometimes been called "atypical resection" or partial resection of the joint. The term "erasion of the joint" is used by English writers, but all these distinctions are confusing. The principal difference between this method and the typical resection of the joint lies in limiting operative interference solely to the diseased structures. In arthrotomy the ligaments and even considerable portions of the synovial membrane may be preserved. In arthrectomy the periosteum and the contour of the bones are preserved, and, if new bone-formation takes place and the repair is all that could be desired, the joint retains it normal outline and sometimes its mobility. It is, moreover, not supposed to interfere with the growth of the limb. The objections to this operation are that it is not thorough, and that it fails oftener than excision to eradicate disease. In twenty-two operations for arthrectomy collected by Muller two patients died of general tuberculosis some months after the operation, in fifteen the wound healed by first intention, there was no shortening in six cases, and in two only was there a certain amount of motion possible. Senn reports two cases of arthrectomy of the elbow-joint, in both of which the "functional result was satisfactory."

The technique of the operation consists in so laying open the joint, as performed in the operation for resection, that its interior shall freely be exposed. This opening is accomplished in the knee-joint by a transverse incision which divides the lateral ligaments. The patella should also be reflected back by free lateral incisions through the capsule, so as to expose the pouch which lies beneath it. The curette is usually not sufficiently effective in removing the tuberculous disease of the synovial membrane, as the diseased layer does not lie loosely over the surface as in cold abscess, but is part of a dense membrane from which it cannot be scraped. Every fragment of diseased tissue must carefully be dissected off with the forceps and scissors. Particular attention should be paid to the various folds of the capsule, and especially to the posterior layer which borders on the popliteal space, taking care to avoid the large vessels that lie very close to the external condyle of the tibia. If the bones are healthy, the synovial membrane alone should be excised; but if sequestra or fistulæ leading to diseased bones are found, it may also be necessary to remove portions of the cartilage and bones. The patella should be allowed to remain if not diseased. Such an operation should of course be performed by the bloodless method and under the strictest antiseptic precautions. After removing the Esmarch bandage the oozing should be arrested by temporary pressure with corrosive sublimate gauze or with iodoform gauze packed into the joint. A few vessels will require ligature, however. If the operator is satisfied that all diseased tissue has been removed, the joint may be closed, a small drain being allowed to remain a day or two in the corner of the wound. Some operators after removing the bandage allow the blood to accumulate within the wound in order that healing by aseptic blood-clot may take place; but this should be tried only when it is desired to fill a space left by the removal of diseased bone, and when it is certain that all diseased germs have been removed. In doubtful cases Krause's method seems the most prudent. This method consists in the tamponade of the synovial cavity with iodoform gauze. All the pouches of the cavity should be filled with gauze which has been freshly rubbed in iodoform powder, and which may remain *in sitû* for a few days or even for two or three weeks. If it is desired at any time to remove the gauze permanently, the joint, if it is still aseptic, can be closed by secondary suture. The dressing may be changed from time to time if the secretion is excessive. Krause adopted this method in two cases of men over fifty years of age in whom there were extensive abscess-formation and burrowing of pus. In both cases healing took place without fistulæ, and the patients reported themselves well a year and a year and a half, respectively, after the operations. Owing to the difficulty of laying open the joint thoroughly, arthrectomy is not well suited to all cases. It is best adapted to the knee-joint, and perhaps also to the elbow-joint, but in the shoulder, and particularly in the hip, the anatomical conditions make it no easy matter to gain access to the more remote portion of the synovial capsule. The preliminary treatment with iodoform, oil, or glycerin paves the way, however, for these more conservative methods of operating, and although they cannot be considered as well established methods at the time of this writing, they have nevertheless a future and deserve a careful trial.

Resection of the joints may be illustrated by a description of the operation upon the knee. The joint is opened by a transverse incision running from condyle to condyle. This cut may be made directly across the centre of the patella, which can be sawn through, or it may curve with the convexity either above or below that bone. Senn makes a curved incision through the skin above the patella, and, after reflecting the flap downward, cuts through the patella, which is united again by suture after the operation. The patella is, however, usually removed even when it is in a healthy condition. After the crucial ligaments have been divided the ends of the bones are made prominent by forced flexion of the limb, and they are sawn off at some point sufficiently removed from the surface to include all the diseased bone. In children the epiphyseal line should carefully be avoided, for, if this is removed, the growth of the bone will greatly be impaired. A thin section, sufficient to include the articular cartilage, is usually all that is needed. Any remaining nodule can subsequently be curetted. The bones must be so cut that the limb will be straight when they are placed in apposition with one another, and care must be taken that the posterior edge of the tibia does not press against the popliteal vessels. After removing the elastic bandage the hemorrhage should be arrested by pressure, by elevation of the limb, and by tying such arteries as require the ligature. The bones can be held firmly together by a silver suture cut short and allowed to remain permanently. It is safer to employ some form of drainage, as in the majority of cases union will be favored by conducting off the serous and bloody discharge of the first few days.

In resection of the hip- and shoulder-joints the operator should not be satisfied with removal of the head of the femur or the humerus, but careful attention must be given to all other portions of the articular cavity, and all diseased tissue must carefully be removed, the incision being made sufficiently large for the purpose. In resection of the elbow-joint it is better to remove the bone freely and to avoid too careful preservation of the periosteum; otherwise ankylosis may occur. The results of such operations are usually excellent, and it is rare that a flail-like joint is obtained.

XXVI. TUBERCULOSIS OF THE SOFT PARTS.

1. Tuberculosis of the Skin.

The identification of many forms of skin disease with tuberculosis has been so satisfactorily demonstrated that no doubt exists at the present time of their true nature.

Among the most prominent of these affections is *lupus*, which is now universally recognized as a tubercular disease, but, before Koch demonstrated the presence of the bacillus of tuberculosis in the lupus nodules, clinical observation had demonstrated the strong probability of its relation to tubercle. Brock found in 79 per cent. of the cases of lupus examined by him complications with other forms of tuberculosis, and Besnier showed that 21 per cent. of his lupus patients died of phthisis. Inoculations in animals have been made successfully from fragments of lupus, and Koch succeeded in obtaining a culture of the bacillus on blood-serum from a case of *lupus hypertrophicus*.

Lupus is characterized by the formation in the skin of minute nodules of a reddish-brown color, more or less transparent and covered with epidermis. They appear to lie just beneath the surface, and they are well defined in outline. A cluster of papules about the size of a pin's head is first observed, and as the organisms grow they gradually approach one another, finally becoming confluent and forming nodules of considerable size. According to the direction which the growth takes there may be an almost infinite variety of forms. The varying degree of involvement of the upper layer of the skin gives rise to differences in the clinical appearances of the disease. These nodules are situated on the cheeks, on the nose, or on some other parts of the face; that is, in an exposed situation. They are very rarely found in the scalp, but are seen occasionally upon the limbs and trunk.

Pathologically, the nodules consist of little granulation tumors in the true skin, in which tumors may be found all the elements of the miliary tubercle. The papillary layer is generally somewhat enlarged. The cutis vera and the papillæ are infiltrated with leucocytes. The collection of cells in the true skin contains well-marked giant-cells. The infiltration in more advanced cases extends sometimes to the adipose tissue. The bacilli are usually hard to find. Cornil and Babes examined microscopally twelve cases, and found a bacillus on only one occasion.

In the ulcerating form of lupus there is a more intense inflammation of the superficial layer of the cutis and the papillæ. The large numbers of leucocytes bring about a softening of these layers, and they break up the attachments of the cells of the rete mucosum. The epidermis, consequently, is thrown off and suppuration of the papillary layer takes place.

The evidence that *lupus vulgaris* is a form of tuberculosis of the skin is sufficiently conclusive. As the disease progresses in the non-ulcerative form the growth takes place from the periphery, and there can occasionally be made out minute tubercular nodules in an early stage of formation. The older portions show a tendency to get well; they lose their peculiar color, the swelling disappears, the epidermis peels off, and cicatricial tissue is left behind.

When the infiltration is not deep the disease appears as a yellowish-brown discoloration of the skin without any elevation of the surface. The diseased part is somewhat softer than the healthy structure, and a probe can easily penetrate the tissue. This form is called "lupus maculosus." Later the nodule may be soft and gelatiniform, or it may contain little masses of colloid material in the form of cysts. In other cases the morbid tissue is very firm and extends deeply into the skin. This form is very slow in its growth, and never breaks down. It is a peculiarly obstinate form of the affection to deal with. In some cases the tubercular nodules seem to be surrounded with an almost cartilaginous induration.

As cicatrization goes on and the upper layers of the skin are destroyed, considerable desquamation occurs: this may be a sufficiently marked characteristic of the affection to receive a special name. This condition is sometimes known as squamous or exfoliating lupus.

When the lupus nodules break down and the cheesy degenerated material is thrown off there is presented the ulcerating type, or lupus exedens. The ulcers are covered with thin brownish crusts and the surrounding skin has a brownish-yellow color. The margin of the ulcer will be raised if the tubercular growth has been an active one. In this type the growth is somewhat more rapid.

When, however, the infiltrated tissues of the skin break down gradually, cicatrization may begin in the centre of the diseased area; and, as the process continues to infiltrate and destroy the surrounding healthy skin a serpiginous ulcer is formed. As the disease proceeds there is sometimes an exuberant formation of tissue which produces a papillary growth. These papillary growths may be developed from granulations which have become covered with epithelium. The names lupus hypertrophicus and lupus framboisioides are given to these forms. When lupus is situated on the lower extremities, the formation of this tissue is so excessive that the limbs are greatly enlarged, forming a species of elephantiasis.

These two principal forms of lupus are not necessarily distinct: the non-ulcerating form may in time ulcerate. The parts become inflamed and softened and ulceration takes place. If ulceration occurs with great rapidity, there may be phagædenic lupus, but this type is exceedingly rare.

Although lupus is principally confined to the skin, it may spread to the deeper parts and the periosteum may be attacked. The disease may spread along the lymphatics and involve the adjacent glands; it may become multiple, attacking several portions of the skin at once. Pulmonary tuberculosis may eventually develop as a secondary complication, but this affection of the skin is a very chronic one, and it usually remains confined to that structure; it may spread, however, to the mucous membranes. Lupus of the face may spread to the mucous membrane of the mouth and the nostrils. The nostrils may become contracted, and sometimes may nearly be obliterated by the cicatricial tissue. The disease may reach the auditory canal and attack the membrana tympani; the conjunctiva, and even the cornea, may become involved in the disease.

Lupus presents certain aspects peculiar to certain localities. On the face the disease begins as the macular variety, and finally forms one or more separate nodules. As these nodules spread and cicatrization takes place extensive surfaces may become involved, and the whole face may be transformed into a cicatricial and discolored tissue. Lupus of the nose generally occupies the tip and the alæ. The reddened and hypertrophied tissue is covered with ulcers and crusts and gives rise to great deformity. The disease is found also on the lips and the external ear. On the limbs and body it assumes the warty and serpiginous forms, and it is frequently accompanied with great hypertrophy of the tissues.

Lupus usually begins in childhood, and with such trifling lesions that it often passes unnoticed until at the period of puberty it springs into new life, and a rapid development of the disease with destruction of the affected part is observed (Van Harlingen).

Tuberculosis vera cutis, which is a rare affection, is usually secondary to disease elsewhere. It starts always from one of the mucous membranes and spreads over the adjacent skin. It begins as minute nodules in the skin that soon break down and ulcerate. A circular or an oval ulcer of variable size is formed. There are usually several ulcers, which may run together and assume a serpiginous form. They are found most frequently near the anus, on the lips, near the nostrils, and on the upper extremities. They are seen only in individuals in advanced stages of pulmonary tuberculosis. They are usually devoid of pain. Esmarch describes such ulcers near the anus, which are, however, very painful, particularly at the time of a movement of the bowels, if they encroach upon the mucous membrane. They may sometimes be quite large and may be multiple. They are usually associated with pulmonary disease, and are probably the result of intestinal infection. The lupoid ulcers described by Allingham are probably of this variety. Leloir lately reported a hybrid affection of lupus and syphilis. In certain cases he found a nodule which healed to a certain point with specific remedies, and then for its entire disappearance required treatment appropriate for tuberculosis.

Scrofuloderma, which is an affection of more frequent occurrence, corresponds to the *gommes scrofuleuses dermiques* of French writers. It is always associated with some other unmistakable signs of general tuberculosis, such as affections of the glands, the bones, or the joints (Zeisler). It is the ulcerated form which is usually said to be tuberculous. The commonest seat of these nodules is on the face, in the submaxillary region, on the neck and thorax, and on the extremities. They are often found near a softened lymphatic gland. They appear at first as a discoloration of the skin, which becomes raised and forms a nodule that spreads slowly, and finally softens at one or more points; or it may appear subcutaneously and gradually involve the skin. Finally small collections of pus form beneath the surface of the diseased skin, which is much discolored. When these cavities open a thin yellowish or sanious pus is discharged, leaving pouches covered with a thin layer of skin. A flat superficial ulcer or a deep fistulous cavity may form in this way. The granulating surface is gelatinous and is of a pale yellowish color. Extensive serpiginous ulcers may thus develop that leave behind them disfiguring scars. Occasionally they coexist with deep-seated nodules of a tubercular nature. They occur at all periods of life, but chiefly at puberty.

There is another class of tubercular lesions of the skin that appear to be the result of direct local inoculation. These types are not usually associated with generalized tubercle, and are essentially local affections. Zeisler classifies under this head four varieties: namely, (*a*) Verruca necrogenica, or anatomical tubercle; (*b*) Tuberculosis verrucosa cutis (Riehl and Paltauf); (*c*) Tuberculosis papillomatosa cutis (Morrow); and (*d*) Tuberculous ulcerations.

(*a*) *Anatomical tubercle*, which is found on the fingers and the dorsal surface of the hand of persons in the habit of handling dead bodies or in performing autopsies, is undoubtedly the result of local inoculation. It begins as a small red nodule, which becomes pustular and is soon covered with a scab. Gradually it spreads on the surface, becomes thicker, and is covered with papillary growths, giving it a warty appearance. It has a well-defined margin. Here and there on its surface are seen small points of pus which can be squeezed out from the deeper layers. In some cases it is quite painful; at times it is very indolent in character. It may spread through the lymphatics to the forearm and the axilla, and in some instances may give rise to a fatal visceral tuberculosis.

(*b*) *Tuberculosis verrucosa cutis* is classified by most writers with anatomical tubercle. It is situated on the dorsal surface of the hands and the fingers and in the interdigital spaces. It varies in size from a dime to a silver dollar. When fully developed a patch consists of three concentric zones. The peripheral zone is erythematous, the color disappearing under pressure of the finger. The second zone is formed of little pustules or of scales covering pustules; the skin is of a reddish-brown color and is somewhat infiltrated. The central zone, which is raised 2 to 3 millimetres above the level of the skin, is covered with papillary growths which are largest at the centre. Between the warty growths are fissures and small skin-abscesses from which can be squeezed a few drops of pus. The growth is very sensitive. The lesion is situated in the superficial layers of the cutis, and it rarely extends to the level of the sudoriparous glands. Riehl and Paltauf found large numbers of the bacilli of tuberculosis in the diseased tissue. The affection is seen in vigorous individuals who are brought by their occupation in contact with domestic animals. It is very slow in development, and it may last from two to fifteen years. Bowen has described examples of this affection. In one case infection occurred in one of the Transatlantic cattle-ships. He also describes a number of cases of this disease occurring in young subjects and on different portions of the body, as on the elbow, the wrist, and the knee. In all cases there appeared to have been a local inoculation. Microscopical examination of specimens taken from some of the lesions showed the characteristic giant-cells and bacilli.

(*c*) The *tuberculosis papillomatosa cutis* is an isolated case described by Morrow, the result of an infection of the skin of the face from pre-existing tubercular disease of the bone. The case was remarkable for the extent and the amount of the warty tubercular growth, which involved the cheeks, the upper lip, the nose, and the eyelids. The hypertrophic condition of the growth and the papillary excrescences were marked features of this case.

(*d*) *Tuberculous ulcerations* produced by inoculation appear on any infected locality. An example of this form occurs in the prepuce after the rite of circumcision when the fresh wound is sucked by the operator and is infected with the saliva. Repeated instances of this form of inoculation have been reported. Infection may occur while washing the linen of consumptives. Brown describes a case of tuberculosis verrucosa cutis on the back of the finger of the right hand of a woman. The disease appeared at the time of the death of a daughter whose soiled handkerchiefs and clothing the mother had been in the habit of washing. Ulcerations have formed after piercing the ears. In all these ulcerations an examination has shown the characteristic giant-cells and bacilli. Most tuberculous affections of the skin, except those seen in advanced general disease, can be cured. Lupus, however, is distinguished from all other tubercular diseases of the skin by its marked tendency to relapse.

The general *treatment* of tuberculosis of the skin is the same in many cases as that adopted for the disease in other parts of the body. Although the general condition of the patient may be good in lupus, in some forms of cutaneous tuberculosis there is more or less cachexia. In any case it is of importance to sustain the patient's health. Cod-liver oil is one of the best remedies for this purpose. Bucq, who considers it the most important internal remedy for this disease, recommends from four to eight tablespoonfuls daily. Among other drugs, arsenic may be mentioned as one of the most efficacious. It may be administered in the form of Fowler's solution.

For local treatment antiseptic agents have been recommended since the nature of the disease has been recognized. White employs a solution of bichloride of mercury, 1 or 2 grains to the ounce, applied half an hour every morning or evening on compresses kept continually wet, or the same drug may be used as an ointment in a strength of 2 grains to the ounce, applied continuously and renewed twice a day. Care must be taken to avoid salivation, which, however, is unlikely to occur if the patient is watched. White noticed rapid improvement at first, and he obtained permanent cures by this method, in some cases after several months of treatment. He also used with satisfactory results from 2 to 4 per cent. solutions of salicylic acid in castor oil.

The objection to this antiseptic mode of treatment is that the agents are not always brought in direct contact with those parts in a stage of active growth. To accomplish this contact it may be necessary to use caustics as a preliminary treatment. Among these caustics pyrogallic acid is supposed to have a mild but effective action. It may be used with ether in a saturated solution on a compress; or it may be sprayed on and afterward covered with collodion; or it may also be employed as an ointment. After the tubercular nodule has been melted down in this way, mercury in the form of a plaster or an ointment may be applied. Iodoform, one of the most effective poisons to tubercle, may be employed locally. It may be applied in the form of a powder or an ointment or in an emulsion with glycerin, or it may be forced into the soft tissues by boring, or it may be injected with a hypodermic needle.

Now that the nature of the disease is known, attempts should always be made to treat it as if it were a malignant growth. Operative procedures are therefore indicated in a large number of cases. There are of course certain regions where excision cannot be performed, as on the alæ of the nose or in extensive disease of the face. The curette or scarificator or the actual cautery may be used in these cases, either alone or as an aid to other forms of treatment.

The soft nature of tuberculous tissue enables the curette to sink easily into it, so that it may thoroughly be scraped away in many cases. It is well to follow up the sharp spoon with some form of caustic. The mildest of caustics is nitrate of silver, which in the form of a pointed stick can be made to search out the various ramifications of the disease. When the diseased tissue is firm and unyielding, it may be exposed by means of scarification, which can be performed with the lancet or by an instrument specially devised for the purpose. After the deeper parts of the diseased tissue have thus been laid bare they may be treated with the antiseptic remedies already mentioned. Scarification is said to leave a better scar than the cautery. In certain parts of the face the actual cautery is one of the most efficient agents for removing the disease immediately without too great loss of tissue. The cicatrization prepared by nature often leaves less deformity than when excision has been performed and an attempt has been made to bring the edges of the wound together by sutures.

Whenever the disease can be excised it is undoubtedly the most efficient way of dealing with it, and is the one least likely to be followed by relapse.

The reputation lupus has for relapse is due to the imperfect methods of eradicating the disease. Even when the wound is so large that the edges cannot be brought together, the surgeon should not hesitate on this account, as there is presented in the Thiersch method of skin-grafting an efficient way of covering the solution of continuity. Large operations of this kind necessitate anæsthesia, but the smaller forms of tuberculous nodule may be excised after local anæsthesia has been produced by subcutaneous injection of a 1 per cent. solution of cocaine.

2. Tuberculosis of the Mucous Membranes.

Only a certain number of these affections are accessible to the surgeon. Primary lupus of the mucous membrane is comparatively rare. In by far the greater number of cases it is secondary to disease of the skin, and proceeds thence to the mouth, the pharynx, the conjunctiva, etc. The small reddish-brown nodules are not observed in the mucous membrane; instead, there are seen minute white points in the livid red and slightly-thickened membrane. There is a superficial loss of cells which can hardly be called ulceration: later these white spots disappear and the surface becomes papillary. Lupus of the pharynx may be seen independently of cutaneous lupus. Ulceration may finally take place, and the ulcers, which last a long time, after partially healing break down again. The ulceration may extend until it involves almost the whole thickness of the mucous membrane.

There are forms of tuberculosis of the throat and soft palate that are not regarded as lupus. This form of the disease is seen as a large superficial ulcer, or ulcers which eventually run together. They have a yellow surface, and they may extend over a large portion of the posterior wall of the pharynx and soft palate. Miliary nodules may be seen lying in the membrane between the ulcers. It closely resembles syphilis, for which it may be mistaken. The extensive adhesion of the velum to the pharynx and the occlusion of the posterior nares are more frequently due to tuberculosis than to syphilis. These cases are often combined with pulmonary tuberculosis, but many cases are amenable to treatment with the curette, with caustics, or with the actual cautery, combined with the local application of iodoform powder.

Tuberculous ozœna occurs independently of lupus, and it appears in the form of ulcerations. This affection is not to be confounded with the ordinary so-called "scrofulous ozœna." The formation of ulcers occurs chiefly on the turbinated bones. They are irregularly shaped with a yellowish purulent surface. They appear to be caused by infection from the pocket handkerchief containing the dried sputa of the patient.

Tuberculous tumors of a polypoid shape are occasionally found attached to the septum. They resemble sarcomata, but they are infiltrated with tubercular nodules. As they grow they may perforate the septum. Their point of origin usually enables one to distinguish them from polypi.

Tuberculosis of the tongue occurs partly in the shape of ulcers which sometimes are torpid and sometimes are of the fungous variety. It appears also as a nodule which breaks down in the centre. Isolated ulcers may be mistaken for cancer, but they can generally be distinguished from that disease by the inflammatory infiltration of the tissues which always accompanies tuberculosis. Volkmann, however, has twice extirpated such growths under the impression that they were cancerous. The nodular form may also be mistaken for syphilis, but in the later stages the cheesy suppuration serves to distinguish it. With the aid of cocaine fragments of tissue can always be removed from the tongue for the purpose of microscopic investigation: the exploratory punch is particularly well suited for this purpose. Examples of this affection are not common in America. The writer has seen but one well-marked case of tuberculosis of the tongue. The apex and about one-third of the lateral half of the tongue were involved in an inflammatory swelling, a portion of which was ulcerated. This case was under observation for several months while the patient was treated with injections of tuberculin. On the borders of the ulcer minute whitish tubercles could be seen during the periods of exacerbation of the disease. In this patient there were slight râles at the apex and a tubercular abscess at the anus. The improvement in the general health was marked during the treatment, and, although after several months of treatment the nodule had not diminished in size, yet a permanent cure was finally effected.

The disease may be treated by excision of a wedge-shaped piece of the tongue or by the actual cautery. In several cases reported by Volkmann there was subsequent pulmonary tuberculosis, although other cases were permanently cured by the operation. In two cases, which he examined post-mortem, the whole surface of the tongue was covered with small flat ulcerations the size of a pin's head, which ulcers in many places became confluent. During life these ulcerations were supposed to be aphthous.

Volkmann has seen non-lupoid tuberculous ulceration of the lip on two occasions. In one case, that of a young girl with multiple cutaneous tuberculosis, the ulcer was removed by a V-shaped incision. In the second case, that of an old woman, the disease had been mistaken for cancer and had been treated with superficial cautery. This ulcer was also excised. A case is reported of a woman, thirty-two years of age, who contracted an ulcer on the inner and outer surface of the lip from her husband, who was suffering from a tubercular ulcer of the gum.

A considerable number of cases of *fistula in ano* are of a tubercular nature. As is well known, this affection is often associated with pulmonary tuberculosis. These fistulæ can be distinguished from the non-specific variety by their tendency to form fungous granulations and sinuses in the mucous membrane and the skin. When these sinuses develop externally their tubercular nature is apparent by the pale, gelatinous character of the granulations and by the reddish-purple color of the thin skin which covers them. They may at times be very extensive, extending out for a considerable distance into the nates. The skin is thin, discolored, and undermined for a considerable distance. On pressure cheesy-like masses and a thin serous pus ooze from the fistulous opening.

As long as the disease is confined to the mucous membrane there appears to be no increase in size of the glands in the inguinal region, but as soon as the margin of the anus or the skin is affected these glands are sometimes found to be enlarged. This affection usually begins in the mucous membrane of the rectum as the result of an infection through some slight bruise or fissure. An ulcer rarely forms here, as is usual in other parts of the intestinal canal when tubercular infection takes place, but the result of this local inoculation is an ischio-rectal abscess. The bacilli are carried through the intestinal canal, as has already been seen, and they are thus brought to this locality. Occasionally a primary infection of this perirectal tissue may occur through an intravascular route, but the disease is most commonly developed secondary to pulmonary or buccal or intestinal tuberculosis. The disease must be treated with the same attention to the necessity of removing all tuberculous tissue as in case of tuberculosis in the bones. The membrane should be curetted away thoroughly, and each sinus should carefully be followed to its termination. The wound should then be stuffed with iodoform gauze. Attempts at excision with subsequent suturing of the wound are more liable to be followed by a recurrence of the disease. The presence of disease in the lungs is not necessarily a contraindication to the operation. In incipient pulmonary phthisis there is no objection to surgical interference, as it is now known that distant parts of the body are not affected by any such operations, as was formerly supposed to be the case. A somewhat analogous form of tubercular infection is observed in the region of the appendix and cæcum. Here also there is a certain amount of stagnation of the intestinal contents, and therefore slight injuries to the mucous membrane are likely to occur. Another peculiarity common to both regions is the presence of loose connective tissue immediately outside the intestine. This tissue is found behind the cæcum as well as around the lower portion of the rectum. For this reason, perhaps, the disease is less confined to the mucous membrane, and it takes the form of an abscess which breaks and leaves a fistulous opening. A certain number of the cases of appendicitis that come to suppuration are of tuberculous origin. In these cases is found a fistula containing fungous granulations which may involve the skin, and it heals with difficulty. Tuberculosis of the mucous membrane of the rectum may occur in the form of small tubercles which break down and form small round ulcers. These tubercles run together, forming ulcers, often of considerable size, that may be recognized by their eaten-out edges, by their irregular surface, and by the presence of fresh gray and yellow softened nodules in the borders, base, and neighborhood of the ulcer. As the disease progresses there may form a circular or girdling ulcer of the rectum which leads to stricture if an attempt is made at cicatrization. In most cases the process spreads slowly and involves the muscular tissue, and perforation may take place into the peritoneal cavity or into the surrounding connective tissue, forming abscesses and sinuses.

Tuberculosis of other portions of the intestinal canal is not infrequent as the result of a primary infection of the membrane by impure food or as the result of a secondary infection from the lungs through tuberculous sputa which have been swallowed. This form of tuberculosis rarely falls to the surgeon's lot to operate upon unless perforation or obstruction should occur, in which case laparotomy, and even intestinal resection, might be called for. One or two such cases have been reported. The result of intestinal tuberculosis is not infrequently an infection of the peritoneum.

3. Tubercular Peritonitis.

Tubercular peritonitis occurs at all periods of life. It is common in childhood, but is seen most frequently between the ages of twenty and forty. This disease is most prevalent among females, although of 21 cases reported by Osler 15 were males, and in 46 cases examined post-mortem in the Munich Pathological Institution 33 were males and only 13 were females.

There are three types of this form of peritonitis: (1) acute miliary tuberculosis of the peritoneum, characterized by a sudden onset, a rapid development, and a serous or sero-sanguineous exudation; (2) chronic caseous and ulcerating tuberculosis, characterized by larger tuberculous growths, which tend to caseate and ulcerate, leading often to perforations between the intestinal coils, and by a purulent or sero-purulent exudation, often sacculated; (3) chronic fibrous tuberculosis, in which the process may be subacute from the outset, or it may represent the final result of the miliary form. Little or no exudation occurs in this variety, and the tubercles are hard and pigmented (Osler).

The peritoneum may be infected, secondarily, through the intestines, the Fallopian tubes, and possibly from the pleura through the diaphragm or from the mesenteric glands. It may also become infected, secondarily to pulmonary tuberculosis, through the circulation. The disease may also occur primarily in the peritoneum, but this is rare.

From the intestine infection may take place through tubercular ulcerations, as there is always a formation of miliary tubercles on the surface of the peritoneum over the ulcers when these reach any considerable size, and from this point a general infection may take place. The bacilli often develop in the lymphatic vessels of the intestine without causing ulceration, and they are carried by these vessels to the mesenteric glands.

In many cases the infection remains localized in some portion of the peritoneal cavity. The commonest seat of this limited tuberculosis is the region of the pelvis in the recto-vaginal or recto-vesical fossæ. When the tubercular virus enters the peritoneum it may be spread about by the peristaltic movements of the intestines or it may tend to gravitate to some one of the pelvic pouches. Localization may be maintained by adhesions of the peritoneal surfaces, which adhesions are sometimes very extensive. The Fallopian tubes are probably a frequent source of tubercular peritonitis, although the tubes may be infected from the peritoneum. Tubercular salpingitis is a complication often found in this disease, for Osler estimates that in from 30 to 40 per cent. of the cases the tubes are affected. In many cases of laparotomy for removal of the tubes these organs are found diseased, while the peritoneum is still healthy. In some cases the disease spreads through the diaphragm and involves the pleura. This complication occurred in only three out of seventeen cases.

When infection takes place through the mesenteric glands they become enlarged, the tubercles making their way through the capsules of the glands, or the diseased glands undergo cheesy softening, and some of the broken-down material is discharged into the peritoneal cavity. Such enlarged glands in young children are often accompanied with distention of the abdomen and marasmus, the condition being known as *tabes mesenterica*. In most of these cases there is probably more or less tubercular peritonitis. Some of these glands may grow so large as to give the appearance of an abdominal tumor. Gardner reports such a case in a man aged twenty-one. Colin describes three cases in soldiers, in whom were found enormous tubercular tumors of the mesenteric glands. In the majority of cases the extension of the process in the peritoneum goes on slowly, and it is accompanied by a formation of connective tissue: in this way thick and extensive adhesions form.

When the omentum is involved in the process the contractions which accompany the formation of adhesions cause the omentum to be retracted into a thick, firm lump, which lies transversely across the abdomen just above the umbilicus. A more or less abundant effusion takes place at the same time. The fluid is either greenish-yellow and turbid, or in more acute cases it may be serous or sero-sanguineous. In some cases the exudation may be purulent in character. Owing to the simultaneous development of adhesions these exudations become sacculated. The omental enlargements and the encysted collection of fluid often give rise to the appearance of a tumor growing at some point in the abdominal cavity. In ninety-six cases collected by Osler of this kind 3 per cent. were supposed to be cases of ovarian or other form of tumor. These sacculated exudations may be found in the upper part of the abdominal cavity, emanating from the region of the liver, the gall-bladder, or the spleen. They may be seen also in the middle part of the abdomen. Here occasionally a cystic accumulation occurs between the layers of the omentum, assuming at times enormous dimensions. Such an accumulation would probably be mistaken for an ovarian tumor.

These exudations may occur also within the pelvis, in which case the disease almost always starts from the Fallopian tube: the coils of intestine immediately become glued together about the diseased spot and shut it off from the general peritoneal cavity. In this way there form extensive pus-cavities which give rise to symptoms of acute inflammation. When the abdominal cavity is opened to relieve these symptoms the intestines are found studded with tubercles. A number of such cases have occurred in the writer's practice, of which cases the following is an example:

A woman twenty-seven years of age had been slowly losing weight for two years when an attack of menorrhagia, with the formation of a tumor in the right iliac region, brought her to the hospital. She remained in the hospital for two months under medical treatment, during which time she improved so much that she was discharged. Eight months later she returned in a bad condition. There was general abdominal distention, a temperature of 102° F., and fluctuation in the right iliac and pubic regions. An incision on the median line showed the intestines everywhere matted together and studded with gray and yellowish nodules, some of which on removal were found to be true tubercles. There was no serous exudation. On separating the pelvic adhesions a pint of very foul pus was evacuated. A drain was left in, and the patient made a good recovery. There was no sign of tubercular disease in any other part of the body. When seen a year later she reported that she was in good health and had married.

The matting together of several coils of intestine may form an almost solid movable tumor not unlike a uterine fibroid. The difficulty of diagnosis in such cases is very great.

Owing to the distortions of the coils of intestines by the presence of adhesions the mucous membrane may ulcerate and perforation may occur. It is quite possible also that symptoms of obstruction may be produced by extensive adhesions of this nature.

Many cases of supposed tubercular peritonitis are not really tubercular. Welch describes fibroid or lymphomatous nodules occurring in chronic serous peritonitis. J. F. Payne describes a case of minute fibrous granulations of the peritoneum associated with growths throughout the liver, possibly syphilitic. A careful examination of the nodules should therefore always be made if possible, and the presence of the bacilli be determined either by the microscope or by inoculation experiments on animals.

Tubercular peritonitis is an affection which shows itself by no well-marked and constant clinical *symptoms.* Its onset is often very insidious. The infection may take place so slowly and so painlessly that the patient may not have presented a single symptom of abdominal disease. The onset may, however, be sudden and be accompanied with all the symptoms of acute peritonitis. Slight fever, occasional vomiting with alternate constipation and diarrhœa, may be the first group of symptoms. On examination of the abdomen the intestines are found distended with gas, and the presence of ascitic fluid may be recognized in the lower portion of the peritoneal cavity. When the exudation takes place rapidly it is often mixed with blood. When the gastric symptoms are very marked the disease may simulate cancer of the stomach. There is often a typhoidal condition which, with continued fever, may lead to the supposition that the patient has typhoid fever; but occasionally there is found a subnormal temperature throughout the course of the disease.

The *prognosis* of the disease is exceedingly unfavorable. It is either an indication that the system is suffering from a general tubercular infection or that disease of other organs may follow in its track. Thus there may be pulmonary tuberculosis as a secondary infection. In the graver forms there may be found extensive amyloid degeneration of the internal organs.

It is now a well-recognized fact that many cases recover spontaneously; it is even possible that the disease may run a latent course, and a cure may take place without a sign of the existence of peritonitis. There is certainly no improbability in the involution of tubercles of the peritoneum as in other portions of the body. The tubercles undergo fibroid and pigmentary induration and the exudation is absorbed. A certain number of adhesions are all that is left to mark the site of the disease. The cases most likely to terminate favorably are those in which the infection is limited to the peritoneum and is of only moderate extent.

The good effects of laparotomy in the treatment of this disease are now generally recognized. In 1862, Spencer Wells performed laparotomy for what was supposed to be an ovarian tumor. He found a tubercular peritonitis. The effusion was withdrawn and the patient recovered. Since then cure has followed many such mistakes in diagnosis. In 1884, Z. B. Adams opened the peritoneum for purulent peritonitis, probably of tubercular origin, and evacuated a large quantity of pus, the patient being alive and in good health ten years later. In a case of exploratory laparotomy performed by Halstead tubercular peritonitis was found, and the cavity was washed out with a sterilized salt solution and drained. The patient made a good recovery. Several months later, the patient having died of pneumonia, an examination showed the tubercles still present and containing bacilli, but undergoing a fibroid change.

The cases best suited for operation are those in which the disease is confined to the peritoneal cavity—those with fresh eruptions and considerable effusion. When the Fallopian tubes are extensively diseased and the tuberculosis has involved the uterus or has spread through the diaphragm, or there is any evidence of pulmonary disease, the conditions are unfavorable. When the purulent stage is reached the chances of recovery are in many cases poor, but the evacuation of circumscribed collections of pus is always indicated unless there is grave constitutional disturbance.

Why laparotomy with drainage produces such a radical change in the peritoneal cavity has not yet been explained. It has been suggested that the curative action is due to the removal of the ptomaïnes which accumulate in the ascitic fluid. The operation undoubtedly produces a profound disturbance in the processes of nutrition of this membrane, and under these circumstances the soil may no longer be favorable for the growth and dissemination of the bacilli. The absorbent action brought about by traumatic inflammation, so common elsewhere, may make itself felt on such an occasion, and it may favor the removal of the broken-down products of the disease.

4. Tuberculosis of the Genito-urinary Organs.

Disease of this region *in women* occurs in about 1 per cent. of all cases of autopsies for tuberculosis (Winckel). Tuberculosis of the Fallopian tubes can occur primarily, but it may also occur secondarily to uterine or to peritoneal disease, or it may accompany disease of the lungs and the intestines. It is found in childhood, but it occurs most frequently in early adult life, and it may follow the puerperal state. Usually both tubes are involved. When both uterus and tubes are affected the tubes are generally more diseased than the uterus. It appears that in most cases the disease begins at the peritoneal end of the tubes, and works its way downward through the uterus to the vagina. The affection begins as a catarrh of the mucous membrane, in which are seen minute gray or yellowish-gray nodules. The canal is more or less distended with muco-purulent material. Ulceration takes place later, and with the breaking down of tissue the tube is filled with cheesy masses. The ulceration may result in perforation of the wall of the tube. In advanced stages the tubes appear coiled and distended and much thickened and indurated. Calcification may take place in the degenerated tissue.

The uterus, as has been seen, is usually affected secondarily to the Fallopian tubes, or the bacilli may enter from the peritoneum through the tubes without involving the latter. In a certain number of cases the disease is undoubtedly primary in the uterus, and it is said to result from the entrance of bacilli during coitus (Councilman). In a case described by Post the patient with a tuberculous testicle had a purulent discharge from the urethra, which on examination was found to contain large numbers of the bacilli of tuberculosis. Tuberculosis may follow the puerperal condition, and it is then found at the site of the placental insertion. In this case it is probable that the disease is transmitted to this region from some point in the interior of the body. Many writers concede an intravascular infection of the genital organs in both sexes. The disease is found in the early stages at the fundus, and it works downward in nearly all cases. In some advanced stages the uterus is enlarged and the cavity is filled with caseous material. The surface of the membrane is roughened and ulcerated, and, although miliary tubercles may be invisible to the naked eye, a microscopical examination reveals the presence of giant-cells and epithelioid cells. The cervix is rarely affected. Cornil and Babes found in six autopsies of cases of tuberculosis of the uterus three in which the bacilli were abundant; they were difficult to find in the other three cases. Their experience in the examination of the tubes was about the same.

The disease in the vagina is most frequently the result of an infection through the secretions which form in the tubes or uterus. It may, however, follow a tubercular peritonitis without infection of the tubes or the uterus. A few cases of primary tuberculosis of the vagina have been observed, but they are exceedingly rare. If the uterus is not involved, the urinary organs or the intestine will probably be found diseased. The vagina may become infected by a perforation of a tubercular ulceration of the rectum through the recto-vaginal septum. Cornil and Babes found bacilli in tuberculous ulcerations surrounding a recto-vaginal fistula, but were unable to find the bacilli in two other cases of tuberculous ulcer of the vagina. The tubercles are seen in the early stages of the affection on the mucous membrane of the vagina as small gray nodules or as larger masses with cheesy, ulcerated surfaces. They are situated in the middle or upper portions of the vagina.

Tuberculosis of the vulva does not appear to be a common affection. Cayla reports a case of tubercular ulceration of the labia and the ostium vaginæ in a case of advanced pulmonary tuberculosis. Cases of lupus of the vulva have also been described. It is conceivable that infection might take place from tubercular discharges both from the vagina and the rectum. In many cases of tuberculosis of the lungs and the intestinal canal the vagina has been found affected, while the uterus and the tubes were in a healthy condition. This fact suggests an infection from the rectum through the anus and the vulva. When an organ is affected with tuberculosis, surgeons are accustomed, in deference to tradition, to assume that the disease has been transmitted to it from the lungs or the intestines. Hegar suggests, in addition to the possibility of a direct infection of the sexual tract during coitus, an infection by fingers and instruments during a vaginal examination. Gonorrhœal infection of the mucous membrane robs it of its epithelium, and a favorable soil is thus offered for the growth and spread of the bacilli. Such gonorrhœal inflammation may spread through the uterine mucous membrane to the Fallopian tubes. In this and in other ways the virus may gradually spread from the original point of infection through the genital tract. It may also be transmitted from the primary lesion through the rich uterine lymphatic plexus to the peritoneum, and thence find its way through the Fallopian tubes into the uterine cavity.

If disease of the uterine tract were suspected, a diagnosis might be established definitely by a microscopical examination of the vaginal secretion, and the presence of the bacilli thus be determined. The enlarged and thickened tubes could be recognized by bimanual palpation. The swollen tube may form a tumor the size and shape of a goose-egg, or it may have an elongated sausage-like feel to the touch. In other cases it may be felt as a series of nodules strung together. In some cases the tubes may be so surrounded and covered by an adhesion and exudation that it is impossible to detect them. Their situation is often changed. They may be displaced into Douglas's cul-de-sac, where they are frequently fastened by adhesions. An enlargement of the uterus might suggest the infection also of that organ. Curetting the inner cavity of the uterus might yield material for a microscopical examination.

The local treatment of tuberculosis of the uterus and the vagina consists principally in antiseptic douches, and in the application of iodoform to the diseased surfaces after the use of the curette or the cautery. Inasmuch as the tubes seem to be affected primarily in the majority of cases, the recognition of tubercular salpingitis before the other organs were involved would be of importance. Laparotomy for the removal of tubes affected with tubercular disease has frequently been performed with satisfactory results.

Tuberculosis of the ovaries is much rarer, according to Klebs, than tuberculosis of the uterus and the tubes, and the former disease does not occur simultaneously with the two last-named affections. Klebs infers that it must become infected, therefore, through the circulation. Quite a number of observers have found diseased ovaries in connection with tuberculous uterine disease. Mosler found tuberculosis of the ovaries seven times in a series of forty-six cases of tuberculosis of the female genital organs. The organs are enlarged to the size of a hen's egg, and are filled with numerous nodules and cheesy masses. Some cases of tuberculosis of ovarian cysts are reported. The surface of the cyst is, in this case, studded with subperitoneal tubercles. In two cases reported the adjacent peritoneum was affected in one and the tubes in the other. Klebs reports a case of ovarian cyst with tubercles on the inner surface in which the infection seems to have proceeded from the uterus. It is not probable that this is the route usually taken, but that the ovaries are affected either primarily or simultaneously with the tubes. If the diagnosis of tuberculosis of the ovaries were made, it would be proper to remove them.

In *tuberculosis of the genital organs of man* the bacilli, according to Cornil and Babes, are not easily found. In cheesy degeneration of the testicles and in epididymis it is often the case that none are obtained. Kocher, however, was able to find bacilli in the periphery of a tuberculous nodule, but not in the pus.

Tuberculosis of the testicle usually begins in the epididymis, and when seen in the early stages it appears as a nodule which is hard to the touch, and in section as a grayish-red, firm, homogeneous mass that has no well-defined boundary, but shades off into the surrounding connective tissue. In this tissue are seen the round or oval or shrunken cylinders of the canals. As the disease progresses a number of these nodules form. The canals are filled with broken-down material and are distended considerably. Occasionally, when these nodules soften, there form in the adjacent tissue small abscesses which frequently break and become fistulous openings.

In the testicles the disease shows itself at first as one or two large nodules which may involve the whole or a large part of the organ. These nodules soften down in the centre and form small abscesses, which also break and form fistulæ. When the testicle is affected secondarily to the epididymis, there are found a number of small nodules in the otherwise normal tissue of the organ. When the whole testicle is involved, a section shows it to consist of the gelatinous homogeneous tissue, in which lie several yellow cheesy masses of stellate or irregular shape. According to Kocher, a microscopical examination of the tubercles in the earliest stage of their development shows within the seminal ducts a collection of giant-cells and epithelioid cells supported between the two layers of the membrana propria and filling out the lumen. The tuberculosis begins, therefore, as an intracanalicular process. As the intracanalicular masses undergo cheesy degeneration the new tubercle is found in the membrana propria. In some cases the membrane seems to be the part chiefly affected, the amount of cell-formation in the ducts being comparatively slight. The neighboring ducts in this case rapidly become involved. In other cases the stroma seems to be the part in which the disease is situated; but as early stages of this process are not seen, it is probable that even the stroma is not in these cases the primary seat of the disease.

In many cases the testicle is no doubt the region in the genito-urinary apparatus where tuberculosis begins. The bacilli have been found in the seminal ducts and in the semen of patients affected with pulmonary tubercle in whom the testicles showed no sign of disease. The organisms are carried to the organ in this case through the blood-vessels, and are transported through the epithelium of the canals into the lumen. The localization of the disease in this organ may be produced by trauma; Simmonds demonstrated this by experiment on a rabbit. An emulsion of tubercular sputum was introduced into the peritoneal cavity of the animal, and a few days later there was produced a contusion of the left testicle. The organ swelled somewhat at first, but the swelling subsided in a short time. Two months later the rabbit was killed, and a general miliary tuberculosis was found, with a broken-down nodule of considerable size in the left testicle. Gonorrhœa is not an infrequent predisposing cause of the disease. In fifty-two cases of tuberculosis of the testicle Kocher found that in fourteen cases the patient had suffered from gonorrhœa. In Simmonds' sixty cases eleven had had gonorrhœa.

The question is often discussed as to the *direction the disease takes in the genito-urinary organs.* Does it ascend from the urethra or the testicle to the kidney? or does it originate in the kidney and descend through the uro-genital tract? Rokitansky and other more recent authorities are of the opinion that the disease ascends from the testicle, but Virchow takes the opposite view. Tubercular disease of the urinary organs is rarely found in connection with disease of the testicle. Tuberculosis of the testicle, although it is rare as a purely primary disease, is often found without tuberculosis of other portions of the genito-urinary apparatus. Primary affection of the kidney, with subsequent disease of the testicle, is not so rare as it is usually supposed to be.

Nevertheless, the usual mode of progression is an ascending one. That is, the disease is transmitted from the testicles to the cord, and subsequently to the prostate. From this point it may be transmitted to the bladder and the kidneys, but this is by no means frequent. An infection of the other testicle occasionally takes place. It is possible that disease of the testicle may give rise to a miliary tuberculosis, and, although this is only a possibility, it is nevertheless to be taken into consideration in deciding upon the propriety of removing the testicle. Salleron, in a series of fifty-one cases of tuberculosis of the testicle and the epididymis, found other organs affected in only one case.

Coming now to the *symptoms* of the disease, it will be found that it is observed principally in youth and in early manhood, but it may also be found late in life. The disease, as has already been seen, begins in the epididymis or the testicle as a painful swelling, which reaches its full growth in a few days or weeks, and it is followed in a short time by the formation of an abscess and the establishment of a fistula which may remain unhealed for several years. The progress is not always rapid, and the swelling may last several months before suppuration takes place. A long interval may elapse before the other testicle is affected. The local tuberculosis may occur without any sign of disease of the lungs or of the urinary organs, although the prostate usually will be found involved.

The vas deferens is frequently enlarged, and it may be felt as a cylindrical cord or as a chain of nodules. This enlargement may extend for a few centimetres from the epididymis or it may be followed to the ring. It is rare that an effusion takes place into the tunica vaginalis. The walls are more frequently glued together by an adhesive inflammation.

The infection of the vesicula seminalis follows disease of the vas deferens. It may also follow disease of the bladder. The walls of the duct are thickened and infiltrated and its cavity is distended with cheesy pus. When in this condition the vesiculæ can easily be felt per rectum: they may reach the size of a walnut. Abscesses may form and discharge both into the rectum and the bladder. Weichselbaum found a perforation of one of the larger veins of the pudendal plexus by a tubercular abscess of one of the seminal vesicles. The prostate is usually affected at the same time, and chiefly on the corresponding side. Abscesses may form and discharge through the perineum.

From the prostate the disease may extend to the bladder and produce multiple ulcerations. The presence of tuberculosis is the cause of frequent and painful micturition and perhaps hæmaturia.

An examination of the urine for the bacilli (see p. 58) will usually settle the diagnosis. *Tuberculosis of the bladder rarely occurs in women:* according to Klebs, it is seen only in the male bladder, as the chance of a progression of the disease from the vagina or the vulva is infinitely less than from the prostate in man.

Tuberculous ulcers, however, have been seen in the female bladder. Albers reports a case of small tubercular nodules near the urethra and in other parts of the bladder. The left ureter was filled with tubercle, and there was tubercular degeneration of the medullary tissue of the left kidney. Winckel, Hewitt, and Scanzoni all report similar cases. Two of Winckel's cases were secondary. In one case the disease of the bladder followed that of the lung; in the other it was preceded by disease of the kidney and the ureter. The kidneys are often involved in the form of pyelitis or of cheesy nephritis.

Tuberculous disease of the testicle is so often followed by abscess and fistula that the *diagnosis* is not usually difficult to establish. The so-called "scrofulous testicle" presents a clinical picture sufficiently characteristic. The scrotum is swollen and reddened, or it is perforated by several fistulæ, and the testicle and its adjacent structures are found thickened and enlarged. When suppuration has not yet taken place the diagnosis is more difficult. The disease can be distinguished from syphilis, as the peculiar stony hardness of the syphilitic testicle is not present. A chronic enlargement of the testicle coming on after a slight trauma or without history of injury is suggestive of tuberculosis, and this suggestion will be strengthened if there is any evidence of tubercular disease elsewhere.

The disease runs a milder course in old people than in early life. It may be confined entirely to the testicle, and may be cured without the involvement of any other organ, but it has been seen that it frequently spreads locally and that it may be followed by miliary tuberculosis. Although it is possible for a cure to take place without operation, the function of the testicle is probably destroyed in all cases. For these reasons the removal of a tuberculous testicle is strongly advocated by most surgeons. *Castration is advised even when the vesiculæ seminales and the prostate are involved*, as it has been observed that disease of these organs as well as of the bladder has undergone speedy improvement, and finally a cure has been effected. Castration is therefore indicated in young people when there are no evidences of advanced kidney or of lung disease. In older people the chance of a cure by local treatment is much better. It has been the writer's experience that many cases, even in young people, when the course of the disease has not been too acute, do well without operation. Andrews states: "I have repeatedly ventured in Illinois, where tuberculosis is far less prevalent than on the sea-coast, to take the patients through the whole affection without other operation than the lancing, drainage, and cleansing of the abscesses; and the patients have ultimately done excellently well and no infection of the lungs or the prostate followed." This experience has certainly been the writer's in several cases. Salleron mentions but two deaths in the fifty-one cases already mentioned. When the local inflammation is severe, however, and there is considerable constitutional disturbance, an operation is advisable. Such a case occurred to the writer recently in an overworked professional man. The testicle was at first much enlarged and there was considerable effusion into the tunica vaginalis. A few months later an abscess formed and the scrotum became greatly swollen and reddened. There were great debility and an evening rise of temperature. No tuberculosis could be discovered in any other portion of the body. Removal of the testicle and a portion of the cord, which appeared to be healthy, was followed by rapid improvement, and the patient now—several years after the operation—is in excellent health. In some of the less acute types of the disease the sinuses may be curretted thoroughly and dressed with iodoform. Careful attention to the general health and to the surroundings of the patient is of great importance. The old-fashioned recommendation of a long sea-voyage is often followed by excellent results. In young adults, however, when the disease comes on rapidly and an enlargement of the prostate and the vesiculæ seminales can be felt in the rectum, castration is certainly indicated.

The presence of tuberculosis of the bladder is a grave complication. In some cases, however, a cure may be obtained by general treatment, combined with such remedies as have a curative effect upon the vesical catarrh which accompanies the disease.

Operative interference is hardly indicated. In the female it would be possible to reach and to cauterize the ulcers by means of vaginal cystotomy. Applications could also be made through such an opening to the diseased surface of the bladder. Suprapubic cystotomy might enable the treatment to be carried on in the same way in man. These operations would, however, be indicated only in exceptional cases.

Tuberculosis of the urethra, a very rare affection, is, according to Kaufmann, always part of a generalized tuberculosis. Infection takes place secondarily from the bladder or the prostate. The prostatic portion is frequently the part affected, and also, but less often, the membranous portion.

Vettesen reports a case of tubercular ulcer of the meatus in a phthisical patient seventeen years of age. There had been painful micturition for some time; an indurated ulcer occupied one side of the meatus and extended inward into the fossa navicularis; the glands in the groin were enlarged; there was enlargement also of the epididymis and the prostate; bacilli were found in the secretions of the ulcer. At the autopsy there was found extensive urogenital tuberculosis: the right kidney, the bladder, the prostate, and the bulbous portion of the urethra were affected.

Englisch describes a tuberculous peri-urethritis in the deeper portions of the urethra. It may exist either inside or outside the deep layer of the superficial fascia. It begins with a discharge of a chronic character from the urethra, followed later by the formation of perineal abscesses and fistulæ. Some of the cases of incurable "watering-pot perineum" are doubtless tubercular in nature. Langhans reports a case of polypoid tubercle situated in the urethra about one inch from the meatus. At the autopsy there were found extensive disease of both kidneys, ulceration in the bladder, and prostatic urethra. It might be mentioned here that Senn reports a case of tubercular ulcer of the dorsum penis that might easily have been mistaken for chancre, and he dwells upon the importance of remembering the possibilities of such a lesion in making a diagnosis.

Tuberculosis of the kidney may occur either as a miliary tuberculosis, as a part of a general infection, or as a nodule or tumor of considerable size. In "nephro-phthisis," as the latter form is called, there are in the renal tissue large caseous nodules which run together, and involve so large a portion of the organ that but little healthy kidney tissue can be found. Frequently the papillæ are the parts first affected when the disease has invaded the pelvis of the kidney from below, the disease working its way along the mucous membrane of the urinary passages. But the pelvis in other cases may become infected secondarily. As the tissue breaks down it is discharged into the pelvis, and the ureter may become blocked with cheesy débris. In this way pyonephrosis may occur. There may be some enlargement of the kidney during the development of the disease, but it is offset by the shrinking of the cavities which form in its interior. Wedge-shaped tubercular infarctions are sometimes found which suggest the lodgment of an infected embolus, probably from the lungs. As the disease progresses there is frequently, as in the lungs, a mixed infection of the pyogenic cocci with the bacilli, and a suppurating inflammation hastens the process of disorganization. When this disorganization is completed the capsule forms a thickened wall or shell, from which spring septa, the remains of the connective-tissue stroma, the capsule enclosing a cavity communicating with the pelvis of the kidney. The walls of this cavity are lined with broken-down tissue and cheesy masses and remains of the kidney structure. When there is great distention from obstruction abscess may form, or rupture into the peritoneal cavity may occur.

The tubercular process may originate in the kidney as the result of tubercular disease in the lungs or elsewhere, or it may be the result of an ascending tubercular infection of the genito-urinary tract. The latter form of origin is far more common in men than in women. Tuberculosis of the kidney occurs at all periods of life, being found in children as well as in adults, but it is commoner in men than in women.

The *symptoms* are those of chronic pyelitis, and they are in no way characteristic of tubercular disease. An examination of the urine, however, shows the presence of bacilli, and occasionally also minute masses of cheesy matter in addition to pus, blood, and casts. If the urine is acid, it is probable that the kidney and not the bladder is affected. Inoculation experiments might settle the diagnosis if the bacilli could not otherwise be detected. The presence of lumbar pains and perhaps of an inflammatory swelling in the region of one kidney, or possibly a tumor, would point to that organ as the seat of the disease. Loss of strength and emaciation, with anæmia, together with hectic fever, would be additional evidence in favor of tubercular disease.

In the exceptional cases of isolated tuberculosis of the kidney—which cases are exceedingly rare—nephrectomy has successfully been performed. If there were indications of the presence of a large pus-cavity in the lumbar region, an attempt might be made to open and drain and to treat the diseased surfaces with appropriate remedies. The tubercular membrane would not, of course, be found in such a cavity, but a great deal of débris could be scraped away, and under favorable circumstances the patient might recover with a urinary fistula. This result, although it exposes the patient to the discomforts of such a fistula, leaves a larger secreting surface than would remain if one kidney had entirely been removed.

5. Tuberculosis of the Mamma.

Tuberculosis of the mamma is a rare disease. Recently Roux succeeded in collecting the records of 34 cases, in 2 of which the disease occurred in males. In 2 cases both breasts were affected. The ages varied from sixteen to fifty-two years. In only 3 cases was an injury supposed to have been the cause of the disease. In 24 cases the disease was secondary to tuberculosis elsewhere. Mandry collected 40 cases, in 21 of which there was histological proof of the tubercular nature of the disease. He found only 1 case in which the male breast was affected, which, he thinks, shows that the functional activity of the gland is important. The ages of the patients in his series ranged from seventeen to fifty-two years. Most of the cases seemed to develop shortly after confinement. In 8 cases the patients had not borne children. In 17 cases the disease was in the right breast and in 8 cases in the left breast. In 7 cases no glands were noticed; in 17 cases there were enlarged glands, and in many of these fistulæ had formed. The glands appear to have been affected secondarily, and not, as König suggests, primarily.

According to Roux, infection appears to take place through the blood-vessels or the lymphatics, or by the breaking of tubercular foci which formed in the adjacent ribs or sternum. Roux also thinks that infection may take place through the ducts, and this appears to have been the mode of entrance of the virus in one of the writer's cases. A tubercular cavity about the size of an English walnut formed near the nipple in a young unmarried woman about twenty years of age. A microscopic examination showed the presence of bacilli. The sinus was treated by curetting and an iodoform dressing, and it healed without further infection of the gland.

According to most authorities, the principal form of tuberculosis of this organ is a primary disseminated or confluent type of the disease. There may also exist an isolated tubercular nodule. There is also the cold abscess in a certain limited number of cases. According to Roux, there may be a secondary involvement of the organ due to disease in adjacent tissues.

The tuberculous breast is sometimes enlarged and sometimes it is smaller than normal. It is often riddled with fistulæ, and the nipple is usually retracted. Pale, flabby granulations protrude from the fistulous openings, and pressure brings out a thin pus with cheesy masses. It contains a number of irregularly-shaped swellings, which on section are found to be indurations of various sizes in which there are irregular cavities with prolongations running in various directions and communicating often with one another. The walls of these cavities are lined with a soft yellowish-gray membrane of varying thickness, and they contain cheesy débris. The surrounding tissue is much indurated, and is dotted over with miliary tubercles. When a large tubercular nodule forms in the breast, a lump is usually seen in the upper and outer quadrant extending to the axilla. The nipple is retracted and the axillary glands are enlarged. These nodules eventually break down and tuberculous fistulæ form. In cold abscess the breast is more or less enlarged by a fluctuating tumor which is situated in the upper and outer quadrant and which appears to be secondary to suppurating glands. The lining membrane of such abscesses is the characteristic tubercular membrane. Miliary tubercles are rare in this situation.

An abscess in this locality was once sent into the writer's ward as a case of malignant disease. An exploratory incision revealed its nature. Another case illustrated secondary infection of the organ. A large collection of pus had formed beneath the gland, and had already burrowed into the breast in several directions. The origin of the pus-cavity was a carious rib. It was necessary to turn up the breast by a curved incision along its lower border in order to reach the diseased bone and to check the burrowing of pus in the mammary gland. In a third case the abscess was situated in the lower hemisphere of the breast of a girl eighteen years of age: a bacteriological examination showed the presence of bacilli in the abscess-walls. The abscess was opened and healed readily under an iodoform dressing.

Under the microscope are found a large number of small tubercles containing giant-cells in and around the tubercular nodules. Clusters of epithelioid cells are found in the interstitial tissue as well as in the acini. Many of the giant-cells appear to originate in the acini, and, according to Bender, they are of epithelial origin, as shown by Arnold to be the case in giant-cell formations in the heart and the lungs.

Patients are not usually aware of the beginning of the disease. Small nodules are accidentally discovered that grow slowly. In fact, the axillary-gland enlargement may have been noted first. As the nodules increase in size the skin becomes involved and the nipple retracts. The disease may last a long time without special change, but finally suppuration takes place and fistulæ form. The development of a cold abscess is almost without symptoms. The disease may be mistaken for a carcinoma which has suppurated or for a submammary abscess. Exploration with the punch or experimental inoculation would in most cases settle the question. In more than half the cases other organs are involved, but the prognosis is favorable if the disease is confined to the breast.

When there is extensive disease of the breast with involvement of the axillary glands, and other organs are not involved, amputation may be performed with a careful dissection of the axilla. Attempts to treat the fistulæ by curetting and the application of iodine are usually followed by a relapse. This clinical experience is in accord with the histological examination, which shows that the disease is not confined to the pus-cavities and fistulæ. In cold abscess curetting may be performed, as in this case the disease is localized. The same treatment may be used for milder forms of the disease when only a limited portion of the gland is involved.

6. Tuberculosis of the Lymphatic Glands.

Tuberculosis of the lymphatic glands is a more common affection than any of those hitherto mentioned. In fact, it occurs both independently and in combination with all the forms that have been described. All those types of disease formerly known as *scrofulous glands* are now recognized as genuine tuberculosis. In the Blegdams hospital in Copenhagen, out of 384 autopsies of children who died of acute infectious disease, 198 showed undoubted tuberculosis, and in all these cases the glands were affected.

The glands of different parts of the body vary greatly in their susceptibility. On the surface of the body the cervical glands are most frequently affected, next the cubital, and less frequently the axillary glands (Volkmann). The glands of the lower extremities are much less liable to disease than those of the upper extremity. Internally the bronchial glands are frequently involved, but the existence of such disease is often overlooked. In children the glands most frequently found diseased at autopsies are the cervical, the mediastinal, the mesenteric, and the retroperitoneal glands. Babes found the cervical, bronchial, and mediastinal glands affected in more than half of all the autopsies performed at the children's hospital at Buda-Pesth during eight years.

When there is a predisposition to tuberculosis, simple enlarged or inflamed glands, due to catarrhal or to cutaneous affections, remain enlarged after these inflammations have subsided. These glands increase in size, soften, and are found, on removal, to be filled with tuberculous deposits. The two principal forms in which tuberculosis appears, large tuberculous foci with cheesy degeneration and miliary tubercles, can both be observed in perfection in the lymphatic glands, though the former type is the one most commonly seen.

When an enlarged gland is removed and is laid open with the knife, there is found hypertrophy of the glandular tissue that shows a pale transparent and uniform surface. In the centre are one or more cheesy masses the size of a ten-cent piece. A careful inspection will show some thickening of the capsule and here and there a miliary tubercle. In a more advanced stage of the disease the cheesy masses soften down, and the cavity thus formed enlarges until nearly all the newly-formed glandular tissue has melted away, and finally the softened material breaks through the capsule of the gland and makes its way to the surface.

A microscopic examination reveals the presence of giant-cells and epithelioid cells around the margins of the cheesy foci. In the miliary form well-marked examples of submiliary tubercle abound. The surrounding tissue shows merely the structure of hypertrophied glandular tissue. In the earlier stages of the process the bacilli are found, often in considerable numbers, as the soil appears to be favorable for their growth, but during the stages of suppuration it may be impossible in many cases to find a single bacillus. Nevertheless, the inoculation of the cheesy material into animals always reproduces the disease.

The most frequent seat of tuberculous adenitis with which the surgeon has to deal is the cervical region. The most common sources of irritation of the cervical glands, particularly in the New England climate, are the prevalent chronic catarrhs of the nose or the throat. Eczema of the face or the scalp, or chronic inflammation about the eyes and the ears, may also be the point of departure of the disease. These inflammations are rarely tubercular, but they produce hypertrophy of the gland, which furnishes a fertile soil for the bacilli. The bacilli are readily grafted upon an inflamed skin or mucous membrane, and they can be carried thence through the lymph-stream to the adjacent glands. The enlarged gland may, however, receive the bacilli from the circulating blood, the organisms having already obtained an entrance to the body elsewhere. The glands enlarge to the size of a walnut, and they can be felt as nodules lying beneath the skin, somewhat tender to the touch, but freely movable. They may remain in this condition for years, and may eventually disappear spontaneously. More frequently they grow gradually, and, by the matting together of several glands from capsular inflammation, form tumors of considerable size. They are usually not painful, and they may remain without further change for a long period. They are not, however, absorbed. At some moment, when the patient's condition has become enfeebled, they begin to soften and to present some of the symptoms of inflammation, and they are much more tender to the touch. It is possible in such cases that a mixed infection has taken place and that true suppuration will follow. More frequently a chronic softening takes place, and fluctuation gradually makes itself apparent. At some point the skin finally becomes adherent to the tumor, changes in color to a purplish red, and finally perforation takes place, there being discharged either tubercular pus or a small amount of pus mixed with cheesy débris, and perhaps calcareous masses. Several such openings may occur, each of which communicates with a separate cluster of glands. The skin becomes undermined, and sinuous fistulæ and pockets are formed which may extend even beneath the sterno-mastoid muscle. The covering to these cavities is a deep red or a purple color, and may be as thin as paper. When the skin is destroyed in this way, tuberculous ulcers form, which after healing leave the unsightly scars so common in tuberculous or "scrofulous" subjects.

The axilla is occasionally, though less frequently, the seat of tubercular adenitis.

A young woman, seventeen years of age and in good general condition, presented herself at the hospital recently for the treatment of a sinus opening on the inner aspect of the short head of the biceps muscle. On probing, the sinus was found to communicate with a chain of glands in the axilla extending beyond the borders of the pectoralis major as far as the margin of the mammary gland. Several operations were performed on this patient: the glands were carefully dissected out, and she left the hospital improved in health. The following winter she returned, hoping to get some benefit from the tuberculin treatment. At this time the disease had not only returned in its original site in the right axilla, but it had also spread across to the opposite side. The supra- and infraclavicular glands on both sides were also involved, and her neck was riddled with tubercular sinuses. There was also marked cachexia. A few weeks later, marked symptoms of tubercular peritonitis having set in, the patient was carried home to die.

The inguinal glands may occasionally also break down and simulate a venereal bubo. The scrofulous bubo, however, is, not associated with any lesion of the genitals. The origin of the glandular enlargement is generally attributed to a sprain. A gentleman consulted the writer for this affection, which he attributed to a strain received while playing tennis. Volkmann reports a case of hemorrhage from the crural artery, the result of the breaking down of a mass of inguinal glands, and also a case of secondary infection of the peritoneum and pleura.

The *prognosis* of tuberculosis of the lymphatic glands is in certain stages of the disease not unfavorable. As has been seen, there is discovered at many a post-mortem examination infected glands whose presence during life had not been suspected. The very large number of such cases leads to the supposition that at a given moment such glands may be present and may subsequently disappear: during the early stage of the glandular affection they are undoubtedly in many cases curable. When, however, the period is reached when several glands have become matted together, forming a visible tumor in the centre of which cheesy deposits have formed, the time has arrived for operative interference.

If operative treatment is carried out before suppuration is established, the glands can be enucleated from surrounding healthy parts. Every effort should be made to remove all fragments of diseased tissue. It is not sufficient to shell out a few of the most obvious nodules: all suspected structures should be dissected away, and the whole diseased tissue should be removed *en masse* if possible. Senn recommends division of the mastoid muscle for the removal of the deeper-seated glands, with subsequent suture of the muscle. The disease should be regarded as one which must be treated by the surgeon's knife as rigidly as if the case were one of cancer. It is also of the utmost importance—and this point is almost invariably overlooked by operators—that the greatest care should be taken to avoid local infection of the exposed healthy tissues. The readiness with which the cheesy products of tuberculosis, when introduced into healthy animals, can reproduce the disease is proof of its virulent power. Carelessness in this respect doubtless explains many cases of relapse after operation. By thorough surgery the patient may not only be relieved of an annoying deformity, but may also escape the dangers of pulmonary or of acute miliary tuberculosis. Many a fatal case of tuberculosis had its origin in the "scrofulous" cervical gland.

When suppuration is established and a cold abscess has developed, it is not sufficient to open the abscess or even to curette carefully its lining membrane. Usually a search with the probe will detect in the deep cervical fascia an opening, on dilating which the remains of an enlarged gland will be found as the source of the suppuration. This gland should carefully be removed, and the healing process will thereby greatly be accelerated. When a small gland softens and suppurates and becomes adherent to the skin, the entire diseased mass can be included between two semi-elliptical incisions, and a clean wound will be left which can be brought together with sutures. When the skin is undermined by superficial pouches or by fistulous tracts, the diseased skin should be trimmed away with scissors, and the tuberculous granulations can then be thoroughly scraped.

The importance of internal treatment in these cases need hardly be dwelt upon. Much may be accomplished in the milder forms of the disease with cod-liver oil, careful diet, and suitable environment. Arsenic is supposed by some writers to have a certain specific action upon these glands. Nothing definite can yet be said on this point, but, as arsenic is also a useful tonic, it is at least worth a trial in cases where there is no great amount of cachexia. Iodide of potassium and syrup of the iodide of iron are also valuable agents in certain cases.

Primary tuberculosis of the connective tissue is rare. In the great majority of cases the disease is secondary to tuberculosis of the glands, bones, or joints. The burrowing of a cold abscess infects long tracts of connective tissue and fasciæ. The primary affection occurs in the panniculus adiposus in small children. A number of small nodules form beneath the skin and run together, involving later the skin itself. These nodules are substantially the *gommes tuberculeuses* already described. Fluctuation is observed finally, and pus is discharged. Volkmann describes these nodules as the furuncular form of skin and connective-tissue tuberculosis. Occasionally the pus may burrow and form a cold abscess quite independent of bone or joint.

7. Tuberculosis of the Tendon-Sheaths.

Tuberculosis of the tendon-sheaths, or tendo-vaginitis tuberculosa, may be either primary or secondary. The secondary form, which occasionally accompanies tubercular disease of a joint, is the variety that has been recognized as tubercular. Later studies have shown, however, that the disease may occur quite independently of any joint disease, and Garré has shown that it is not so rare as has been supposed. This observer met with twenty-five cases of the disease in seven thousand cases seen by him in two and a half years.

This disease occurs in two forms. The *fungous* form is characterized by the formation of an exuberant granulation tissue, which at times assumes the characteristic gelatinous appearance and envelops the tendon within its sheath. At other times growths occur on the inner surface of the sheath, which growths become detached, forming the so-called "rice bodies," "melon-seed bodies," or corpora oryzoidea, as they are variously styled. This affection, known as *hygroma*, was supposed to be quite distinct from tubercular disease, but it is now definitely established that the greater portion of these bodies contain tubercle bacilli. Similar bodies are found in the mucous bursæ, and it has been proved, of some of them at least, that they are tubercular. These same bodies are found also in joints (hydrops fibrinosus), and they develop from the fibroid degeneration of tubercular granulations. There has been a great deal of speculation about these peculiar structures from first to last. Dupuytren, for instance, thought that they were hydatids, but the careful histological studies of late observers have definitely established their true nature.

Primary tuberculosis of the tendon-sheaths occurs chiefly in adult life. It is commoner between the ages of thirty and forty than at any other period. The affection seems to follow some injury or sprain, and it is seen most frequently in laboring people. The right side is more frequently affected than the left, and the flexors more frequently than the extensors. In the fungous form of the disease the sheath of the affected tendon is lined with a grayish-red, highly-vascular tissue, which forms a long cylindrical rather firm connective-tissue growth. This growth distends the sheath of the tendon, and it is sometimes firmly attached to the tendon itself, the growth having penetrated its fibre. At other times the tendons can be dissected out clean from this tissue. The cavity of the sheath is usually not entirely obliterated, and occasionally rice bodies may be found in it, showing the relationship of this form to the other variety of the disease. The fungous growth may extend beyond the sheath of the tendon and invade the muscle. This complication is sometimes seen in the peroneal tendons. When examined under the microscope the walls of the tendon-sheaths are found thickened by a small-cell infiltration in which are found giant-cells. The fibrous layer of the sheath gradually disappears, and it is replaced by fungoid granulations. The visceral or peritendinous layer is also often affected. The tendon in this case appears to be thickened, and its sheath is covered with a fibrinous exudation. Under the microscope there are seen on the surface tubercular products in a state of fibrinoid degeneration. Beneath these products there is a layer of highly-vascular granulation tissue containing giant-cells, and next the tendon there is either a loose connective tissue or the granulation tissue has penetrated into the substance of the tendon itself (Garré). The number of tubercles varies: sometimes they are found quite numerous and arranged in rows, each one being encapsuled in a ring of connective tissue. If the cavity of the sheath remains well defined, there may be seen several layers of endothelium upon it, but this is often worn away at the points of greatest friction, and there are found papillary granulations which probably are the beginning of the rice bodies.

In the hygroma type the inner surface of the cyst has slight excrescences which have undergone fibrinoid degeneration. By friction these excrescences become pediculated, and they are entirely separated as rice bodies. They consist of a stratified or a structureless fibrinoid tissue which contains only a few cell-nuclei, but here and there is a giant-cell with tubercle bacilli. These bacilli are still capable of growth, and when the rice bodies are introduced into the tissue of animals tuberculosis may be produced. In many cases the inoculation fails, showing that active bacilli are not always found in these bodies. The disease, thus produced, develops slowly, demonstrating that it takes a certain amount of time for the bacilli to be liberated from their somewhat dense capsule. The wall of the hygroma cyst is also found to be in a state of tubercular degeneration. Isolated tuberculous tumors are occasionally seen in the tendon-sheaths, similar to those already spoken of as occurring in the joints and in the nasal cavity. The cell-growth in these tumors is so large as to suggest in some cases sarcomatous tissue.

The *symptoms* of the disease are quite chronic in character, and they develop very slowly, usually dating back to some injury. The swelling found at that time does not go down, but rather increases in size and becomes painful. The tumor is flat, oval, or sausage-shaped, and it is soft, elastic, and pseudo-fluctuating. In the case of hygroma the fluctuation is quite distinct. When the diseased tendons run beneath an annular ligament a constriction is found, giving the tumor an hour-glass appearance. The palmar bursal tumors of the hand belong to the hygroma type of the disease, and pressure above and below the annular ligament forces the rice bodies to and fro in a manner quite characteristic. The skin is not involved at first, but later, when suppuration occurs, it may become infiltrated, and ulcers and sinuses eventually are formed. This is more commonly the case in the fungous type. True cold abscess is rarely seen. When cicatricial contraction sets in the function of the tendon may seriously be interfered with. If the hygroma breaks externally, acute suppuration may follow, which greatly impairs the use of the hand. In some cases the joint over which the tendons run may become involved in the disease.

The tendons most frequently affected are those situated on the palmar and dorsal aspect of the wrist (Fig. 82). In the neighborhood of the ankle-joint is found the fungous form in the perineal sheaths, and also in the tibialis posticus and the extensor communis digitorum. Ulceration occurs here earlier than in the hand. The plantar surface of the foot is not affected. In the neighborhood of the knee-joint some of the tendons may be affected with this disease, but here it is much less common.

Fig. 82.—Tuberculosis of Tendon-sheaths or Palmar Bursal Tumor.

Secondary tubercular disease of the tendon-sheaths is almost always of the fungous type. It is important to recognize this complication in operations upon the joint: otherwise the diseased tissues may be overlooked. The differential diagnosis between the primary and the secondary forms is often hard to settle if the joint happens to be affected.

Fatty tumors are also rarely seen in the tendon-sheaths under the name of lipoma arborescens. Sendler reports such a case in a girl fourteen years of age. The tumor occupied the sheaths of the extensor tendons of the hand, and when removed it appeared as a reddish-yellow lobulated mass of fatty tissue with prolongations extending to each tendon. Three months after the operation the patient died of pulmonary tuberculosis. Although in these cases the presence of tubercles does not appear to have been established by the observers, it is probable that these forms closely resemble the same tumor observed in the knee-joint in which miliary tubercles are found. Moreover, in another case there was a family history of tuberculosis, and in a third the patient was suffering from cachexia.

Many of the forms of primary tuberculosis of the tendon-sheaths may be treated by excision of the diseased mass.

A lady sixty years of age consulted the writer for tuberculosis of the sheaths of the peroneal tendons at their point of contact with the external malleolus. The disease extended nearly to the point of their insertion and some distance above the malleolus. She had suffered in her youth from caries of the rib. The tendons were exposed by an incision about five inches in length, and a long spindle-shaped gelatinous mass was carefully dissected out, leaving both tendons clean and bright. The wound, which was complicated by sinuses, healed slowly by granulation. Perfect motion of the joint was obtained.

When the elastic tourniquet is applied these operations can be performed without hemorrhage and an elaborate dissection can be made. In the palmar bursal tumor the annular ligament may be divided, if necessary, and the tendons dissected out one by one. During the healing process the tendons appear to form new sheaths for themselves in the granulation tissue, and the function of the tendons usually is but slighty impaired by the operation.

When this condition is secondary to joint disease the operator must pay careful attention to this complication in performing resection of the joint. When resection is not indicated amputation is probably the only resource if the general condition of the patient will permit of such an operation. The prognosis is favorable in primary disease of the tendon-sheath, as the fibrinoid type of tuberculosis is not likely to be followed by metastasis.

Tuberculosis of muscular tissue is very rare. A muscle may, however, be affected secondarily to disease of an adjacent bone.

8. Scrofula.

Scrofula is a name that was formerly given to a large proportion of the affections just described as tuberculous disease, and the question naturally arises whether there are any affections which should still be classed under this head. The name is derived from *sus*, *scrofa*, a sow, to indicate the peculiar fulness which the enlarged lymphatic glands give to the neck. As is now known, these glands are tuberculous, but there still remains a class of inflammations that are not tuberculous in character, to which certain children are liable, and which some authors are still inclined to include under the head of scrofula. Landerer describes two types of scrofulous patients—the *torpid* and the *erethitic*. The former is the type generally recognized in the so-called "scrofulous child." The complexion is usually of a pale blond or pasty hue; the hair is frequently red; the features are coarse, the eyes watery blue, the lashes long, the lips thick, the nostrils large, the expression dull, and the figure inclined to plumpness. There is a tendency to chronic inflammations of the eyelids or of the cornea. There is often nasal catarrh, with fissures about the lips and nostrils, and pharyngeal catarrh, with enlargement of the tonsils. Such patients are also afflicted with chronic inflammation of the ear, and are likely to have eczematous eruptions of the face and scalp. The glands of the neck are almost always enlarged. Such children have a tendency to catch cold easily, to suffer from bronchial catarrh, and they are a constant source of anxiety.

In the second type the erethitic, the children are of dark complexion, nervous and restless. They possess the tendency to succumb easily to conditions by which healthy children would not be affected. There is less tendency to enlargement of the glands, but the same susceptibility to chronic inflammatory processes exists.

This seems a somewhat fanciful sketch. There is, however, this foundation for it: namely, that there exists a type of children who are subject to chronic inflammatory infections, and who, although they may not have an inherited predisposition to tuberculosis, nevertheless are more susceptible to the virus than are those who have sound constitutions. It is possible, moreover, that many of these inflammations, and even glandular enlargements, may be due to other microbes than the bacillus of tuberculosis, and the observations and experiences of quite a number of observers appear to strengthen this opinion.

Charrin and Roger studied an organism which produces a lesion similar to that produced by the bacilli of tuberculosis. They found in the liver and spleen of a guinea-pig which died in the laboratory, not having been the subject of experiment, numerous minute granulations resembling miliary tubercles. On taking gelatin cultures from these they obtained at the end of forty-eight hours a whitish growth which grew for a few days without liquefying the gelatin. Under the microscope the organisms appeared as movable bacilli from 1 to 2μ in length. Inoculation of animals subcutaneously produced a local tumor containing cheesy matter and accompanied by a swelling of the adjacent glands. At the autopsies the spleen and kidneys were found enlarged and full of miliary nodules. A large number of experiments with this organism were followed by a constant result. Pfeiffer describes also a short bacillus which when introduced into mice produces enlargement of the adjacent glands and nodules in the spleen and liver, and also in the intestine.

Cornil and Babes report two cases occurring at Bucharest of acute bronchitis accompanied by the formation of miliary nodules. In the first case there was also intermittent fever. At the autopsy miliary tubercles were found around the bronchi, which tubercles, when examined, were found to contain chains and clusters of oval microbes about 0.8μ in size. Cultures in gelatin produced a foul-smelling bacillus about 0.6μ in length. In the second case, in which there was no malaria, the same organisms were observed.

Malassez and Vignal as early as 1883 described under the name of tuberculosis zoöglœica a disease microscopically resembling tuberculosis. In the centre of the nodules were found large zoöglœa masses of a variety of different organisms, but no bacilli of tuberculosis.

Zagari obtained gelatin cultures at ordinary temperature from tubercular nodules in a guinea-pig. A fragment of this culture introduced into the subcutaneous cellular tissue of another guinea-pig reproduced the same disease and the same organisms. Each nodule under the microscope appeared to consist of a collection of small round-cells, "infiltration" cells, and leucocytes. The borders of the nodule were not well defined, but the growth spread irregularly into the surrounding tissue. Other nodules showed the epithelial type and occasionally also giant-cells. Signs of hyaline degeneration were found in the nodules and also in the neighboring tissue. In the centre of each nodule was a mass of peculiar granular consistency which appeared like cheesy material. By a somewhat complicated method of staining it was found that these central masses contained bacilli with rounded ends, 1μ long, and also oval bacteria from $0.4–0.8\mu$ long and about 0.3μ wide. In the centre were long chains and threads; at the periphery were short bacilli and isolated micrococci. In the surrounding granulation tissue there were small groups of micro-organisms, some of which were micrococci and some diplococci, arranged in coils or straight lines—

all apparently phases in the growth of the same organism. After frequent inoculations the type changed to a finer miliary nodule. To reproduce the coarser nodules it was necessary to introduce small amounts of the culture into the intestinal canal or to subject the organism to the drying effect of the air, or to a lower temperature, or to a struggle with other organisms. Zagari thinks that this virus, which is evidently widely spread in nature, should be studied with reference to its occurrence in man. Some of the cases of peritonitis reported above were found not to be genuine tubercular disease.

It is highly probable that further study will show that the bacillus of tuberculosis is not the only organism capable of producing this type of chronic inflammation in man. Surgeons are, in fact, still but on the threshold of this line of investigation.

XXVII. DISEASES OF BONE.

1. OSTEOMALACIA.

OSTEOMALACIA is a disease of the bones in adult life that occurs most frequently in puerperal women, but it is seen also in women who are not in the puerperal state and in men. It is characterized by a progressive softening of the bone-substance, giving rise to deformity and sometimes to fracture. The first change noticed in osteomalacia is a gradual *absorption of the lime-salts* from the outer

FIG. 83.—Trabecula of Bone in a case of Osteomalacia—on the left osteoclasts, and on the right osteoblasts (oc. 3, obj. D.).

layers of the trabeculæ or those layers in direct contact with the medullary tissue. The portion of the bone thus decalcified is composed of fibrous or striated tissue in which are found the bone-cells:

these cells, however, have changed somewhat in shape, having lost their prolongations, and some of them having entirely disappeared. The outline between the bony tissue which still remains in the centre of the trabeculæ and this altered tissue, which may be called "osteoid tissue," is said to be well defined. Sometimes the trabeculæ become quite irregular, presenting indentations or the so-called "Howship's lacunæ." The bony trabeculæ become narrower and narrower, and they may disappear entirely as the disease advances, leaving the osteoid tissue, which in its turn may be absorbed by the action of the osteoclasts. In case of improvement, however, the lime-salts may be deposited again and the trabeculæ may assume their former condition. In well-advanced stages of the morbid process destruction and repair may be seen going on simultaneously, the osteoclasts causing absorption of the bony tissue, and the osteoblasts formation of new bone (Fig. 83).

In the mean time the *medullary tissue* throughout the bone is undergoing a marked change. The fatty tissue of which it is mostly composed in adult life is infiltrated with round-cells, and there is also hyperæmia of the blood-vessels; which affection changes the tissue into one resembling the red marrow of infancy. This tissue appears to take on active growth and to deprive the surrounding bony trabeculæ of their lime-salts, and subsequently to break up and absorb the decalcified bone. The trabeculæ of the spongy bone are gradually absorbed, the Haversian canals become wider, and the cortical bone is soon converted into spongy bone. As the bony tissue gradually melts away there is little left but marrow and periosteum if the process continues long enough (Fig. 84). Bones in which the disease has made much progress become, therefore, soft and yielding, and they are easily twisted out of shape or are broken, and they can readily be cut through with a stout knife. The cortical layer of a long bone like the femur sometimes becomes as thin as paper, and its marrow has a red, succulent, spongy look. Numerous hemorrhages often occur in the vascular medullary tissue, and pigment is deposited. This new tissue may at any time undergo mucous degeneration, many of the cells disappearing and a gelatinous intercellular substance taking its place, or it may appear as a yellowish fatty tissue. In some cases the gelatinous softening takes place to such an extent that cysts form, sometimes of considerable size. Later it may resume its medullary activity and continue the destruction of the bone, for it would seem that it is owing to this unusual activity of the medullary tissue that the bone is deprived of its salts and is absorbed.

Although osteomalacia is regarded as a degenerative process, the changes seen in the cellular structures closely resemble an inflammatory process, so far as the formation of a granulation tissue is concerned; but there is not found other evidence of bone-inflam-

FIG. 84.—Section of Femur in a case of Osteomalacia: below is the medulla rich in cells, and above, the periosteum (oc. 3, obj. A.).

mation, such as the formation of new bone. One indication of a disturbance of nutrition is *the chemical change seen in the bone* in this disease. The presence of lactic acid in excess in the bones affected has been supposed by several writers to be the cause of the absorption of the lime-salts. At certain periods of the disease lactic acid has been observed in the urine. This acid was found to diminish greatly in the cases reported during convalescence, and to disappear entirely with cure. Lime-salts have been found to a very limited extent in the urine. A chemical examination of the bone shows marked diminution of the gluten, and there has been found in the urine an albuminous substance which has been supposed to be connected in some way with this change. The significance of these chemical changes, however, has not been sufficiently determined to throw any light upon the origin of the disease.

It has been thought possible that the disease might be of bacterial origin, owing to the fact that it is often found in damp dwellings and it has followed sudden drenching of the clothing. Animals improperly fed and kept in damp stalls have also suffered from the disease. In a certain prison in Prague the disease appeared to prevail. It is, in fact, more frequent in certain localities than others, and it is observed frequently in Bavaria, Westphalia, Alsace, and along the borders of the Rhine, but in other parts of Germany it is extremely rare. It is rarely seen in England and in America. According to Busch, in 1888 only one hundred and sixty cases of this disease had been reported. Eighty-five of these cases were women in the puerperal state, and all were between twenty and forty years of age. Frequent pregnancies and long nursing, with poor opportunities to obtain proper nourishment, seem to have been the condition most favorable for the development of the disease in these cases. An analysis of these cases shows that the pelvis and the spine are the parts most frequently affected, far more so in puerperal cases than in non-puerperal women and in men. In the latter class all regions of the skeleton were affected, but in both classes of cases the disease was found less frequently in the head than elsewhere.

Fehling attributes the disease to a pathological increase in the activity of the ovaries, in consequence of which there is a reflex action exerting itself upon the vaso-dilators of the blood-vessels of the bones. As the result of this there is hyperæmia, under the influence of which an absorption of bony tissue takes place. This view is based upon the fact that a marked improvement of the disease has followed removal of the ovaries. Fehling regards osteomalacia, therefore, as a reflex tropho-neurosis of the osseous system proceeding from the ovaries. Winckel and others who have had experience in ovariotomy for osteomalacia do not accept this view.

The *symptoms* of the disease begin usually after confinement. The patient complains of acute pain in the pelvis and in the lumbar region, with radiating pains down the thighs and up the back. They are more severe at night, and continue throughout the progress of the disease. The morbid change almost always begins in the iliac bone in puerperal cases. Pressure or movement seems to aggravate the pain, which is brought on by the weight borne upon the pelvis when in the sitting posture. As the disease spreads and involves the spine and the inferior extremities, standing and walking become painful. The deformity of the bones now becomes apparent. If the spine curves forward, there is *lordosis;* if the curve is backward, there is *kyphosis*, and with this malformation the ribs are often pressed in upon the spine. There may also be lateral curvature, or *scoliosis*. The vertebræ are compressed by pressure against one another, and the stature of the patient is in this way often materially diminished. The deformity of the pelvis consists principally in an approximation of the acetabula. The promontory of the sacrum and the symphysis pubis are brought close to each other. In the long bones fracture often occurs.

The deformity of the pelvis is so great that in subsequent confinements, notwithstanding the softening of the bones, normal delivery cannot take place, and ovariotomy or Cæsarian section must be performed. In the extremities the softening of the bones permits of their being twisted about in every direction. If respiration is not interfered with, the internal organs usually perform their functions well. In severe forms of the disease there may be bronchial catarrh and diarrhœa with cachexia. In some cases there is often a spasmodic action of the muscles, and sometimes convulsions. Fever is not present at first, but in the later stages a hectic fever may establish itself in case of inflammatory complications. A remission of the symptoms often occurs after recovery from a confinement, but with the return of pregnancy the disease reappears. The intellect does not seem to suffer.

The section of bone shown in Figures 83 and 84 was taken from a case of spontaneous fracture of the left femur. The patient, a native of Ireland and twenty-two years of age, was confined twenty-two months before, being delivered of a seven-months' child. Since then she had suffered from stiffness of knee and pains in the thigh of the left limb, and also in the right limb. The record of the case does not state the cause of fracture, which was at the junction of the upper and middle thirds of the femur. The bone failing to unite and there being suspicion of malignant disease, the thigh was amputated. The next day a fracture of the right thigh was discovered, which united without delay, but six months later the patient was still unable to stand upon it.

The *prognosis* of the disease appears to be extremely unfavorable, particularly in its puerperal form. Of 87 such cases reported by Lietzmann, 60 died, although it should be said that a majority of these cases died of complications occurring during confinement. The duration of the disease may, however, be long, varying all the way from two to ten years. The prognosis is somewhat more favorable in non-puerperal cases. In its early stages the disease may be mistaken for rheumatism or for syphilis, owing to the peculiar osteocopic pains. With the appearance of deformities in the bones or of fracture there is usually little doubt as to the diagnosis, although it may be supposed that some of the bony displacements are caused by the presence of malignant disease.

In the *treatment* of osteomalacia there appears to be no therapeutic agent which seems to exert a beneficial effect upon the condition of the bones. The remedy which has most often been used—namely, the phosphate or carbonate of lime—is thought by some to be worthless and to throw additional work upon the kidneys; but the fact remains that there is an unusual drain upon the system of these chemical substances, and an artificial supply may at least tend to restore the desired equilibrium. The employment of food rich in lime-salts, such as vegetables, fish, and meat, and porter, is recommended. Careful attention to the diet is probably the most important requirement in the management of the case. Cod-liver oil (with or without phosphorus) and iron are tonics frequently recommended for this affection. They have no specific action upon the processes going on in the bone, but they serve the purpose of maintaining the patient's strength, and thus placing the system in a condition more favorable for reparative processes. Women should be warned of the dangers of a second pregnancy.

Recently ovariotomy has been performed for this affection. In the early Porro operations, which were performed on women with rachitic pelves, it was found that a rapid improvement of the disease followed the operation. It occurred to Fehling, therefore, to try the effect of the removal of the ovaries. Winckel proposed that the operation should be limited to such cases where all other methods had failed and the patients had already had many children. The first operation of this kind was performed in 1887, and since that time 41 cases have been operated upon, with 5 deaths, or a mortality of 12 per cent. Of these cases, 2 died of sepsis and 1 of fatty degeneration of the heart.

A marked improvement was observed very soon after the operation, but it was not always permanent. The pains in the bones, particularly in the pelvis and thighs, were greatly relieved. The ability to walk came more slowly. In the majority of the cases there was permanent cure. In the case of pregnancy Porro's operation—or, as a substitute, Cæsarian section combined with ovariotomy—may be performed. In the great majority of cases

Porro's operation (removal of the uterus and ovaries) is the one which should undoubtedly be chosen.

2. RICKETS.

Rachitis, or rickets (ῥάχις, a spine), is a disease of infancy and childhood characterized by a disturbance of nutrition and an irregular development of bone, causing a change in its composition, texture, and form.

The period of life at which this disease is most commonly seen is in the first and second years. In a series of cases compiled by Bradford and Lovett, 710 occurred in the first year, 831 in the second year, 232 in the third year, 50 in the fourth year, 27 in the fifth year, and after that period 26 cases only. It seldom begins before six months or after three years. Rickets is occasionally seen in individuals at the age of puberty, although the affection at this period is rare.

It is an old theory that rickets is due to an abnormal development of acids. Heitzmann suggested that it may be due to the presence of lactic acid. This acid is supposed to be formed in the body as the result of digestive disturbances, acting as an irritant on the bone-forming tissues and causing solution and excretion of lime-salts. According to other authorities, the absence of lime is explained by its insufficient administration in food. Kassowitz called attention to the great vascularity of the medullary tissues in rachitic bones, and he sought in this condition of the bone an explanation of the disease, which he assumed was due to inflammatory hyperæmia of the osteogenic tissues.

Pommer, seeing the early and frequent disturbances in the motor system in this disease and the frequent complications of the nervous system, advanced the theory that the disease has its origin in the central nervous system. According to Monti, the cause of rickets lies in a defective nutrition of the affected children. All forms of nutriment which cause dyspepsia, and consequently malassimilation, or which do not contain the proper nutritive elements, bring on rachitis. The artificial feeding of children with patent foods has been thought to be a fertile source of the disease. In menageries, where animals live under highly artificial conditions, rickets is often seen.

Any disease or condition of life which favors debility in an infant serves as a predisposing cause. Bad hygienic surroundings, damp dwellings, crowded tenements, and poor ventilation are conditions under which the disease seems to thrive. Acute febrile diseases, such as pneumonia, scarlet fever, and measles, are frequent forerunners of rickets. Rickets is not so distinctly an inherited disease as one resulting from an enfeebled condition of the parents engendered by constitutional affections, such as syphilis or tuberculosis, or as the result of poverty.

Rickets is common in Northern and Middle Europe, and especially in England. In America the disease is neither very prevalent nor severe, and, except in negroes, Italians, and Portuguese, very great deformity is rare (Bradford). According to Stedman, it is much less common among the children of Irish parents, but negroes are, almost without exception, rachitic. The disposition in the colored race seems to be an acquired one, for it is said that native Africans seldom, if ever, show any evidence of the disease.

Rickets may develop during intra-uterine life (fœtal rickets), or it may begin then and develop fully after birth (congenital rickets).

The principal *pathological change* is seen at the epiphyseal lines of long bones and beneath the periosteum. It consists apparently in an insufficient supply of lime-salts to the bone, and is characterized by an extensive absorption of bony tissue and the formation of bone without lime-salts, or the so-called "osteoid tissue."

A description of the normal ossification of long bones at the epiphyseal line serves to make clearer the peculiar changes seen in rickets. Near the line where cartilage and bone come in contact are seen the cartilage-cells beginning to increase in numbers, and as this line is approached they are arranged in columns. Arriving close to the line, these columns are found to contain cartilage-cells closely packed together and much increased in size. These changes are characteristic of active growth in the cartilage. At the line of junction with the bone it is found that the further growth of the cartilage is arrested by the deposition of a narrow layer of lime-salts. Directly below this calcified layer is the medullary tissue of the bone, with its loops of blood-vessels pushing up against the calcified zone, which it presently absorbs. The cartilage-cells lose themselves in the advancing medullary tissue, some of them probably becoming marrow-cells. As these finger-like processes of vascular tissue push their way up into the cartilage, the trabeculæ of cartilage left between them are partly absorbed, and partly changed into bone through the agency of osteoblasts which form around them.

The most marked divergence from this process in rickets is the absence of the calcification-line which is so constant and so characteristic a feature of the normal growth of bone. In severe forms it is wanting entirely; in moderate rickets traces of it may be found here and there. The next most important change—and one that never fails—is the increase in size of the zone of active cartilage-cell growth. The columns of crowded cartilage-cells extend over a much greater area than normally. The third important change is the formation of the most irregular and enlarged and highly-vascular medullary spaces, which grow up into the cartilage in the most tortuous shapes (Ziegler). The white line of calcification between cartilage and bone is therefore wanting; the growing cartilage forms a very broad transparent layer, and the boundary-line between cartilage and bone is most irregular. Patches of cartilage are consequently seen still unaltered much below the upper edge of the bony tissue. The rest of the cartilage, as it is gradually enveloped by the vascular medullary tissue, changes into osteoid tissue. A zone of osteoid tissue—that is, bone which has not yet become calcified—is formed beneath the cartilage. This zone is consequently more or less soft and yielding, and it has a tendency to bend under pressure.

These osteoid trabeculæ have no regular form or arrangement like the normal bony trabeculæ. Still lower down are found lime-salts deposited in the central axes of these trabeculæ, and in this way a layer of partially ossified substance is formed. In the periosteal layer of growing bone spongy bone-tissue forms, partly by the absorption of old bone and partly by the formation of osteoid tissue, so that when the disease is well advanced the surface of bones is covered with a highly vascular tissue which offers resistance to firm pressure, but which can easily be cut with a knife.

While in this stage of the disease the condition of the bone resembles strongly that seen in osteomalacia; the difference lies in the process. The layer of bone which has no lime-salts in it is, in the case of osteomalacia, decalcified bone; in rickets it is newly-formed osteoid tissue. The bone which contains lime-salts is in osteomalacia always old bone; in rickets it is partly old and partly newly-formed bone (Ziegler).

As a result of the disturbance of the process of ossification there is thickening of the ends of the bones, caused by a growth of epiphyseal cartilage. The periosteal growth of uncalcified osteophytes causes a thickening of the shafts of long bones and of the outer table of flat bones. When a cure finally takes place the bones appear unusually thick and heavy. The bones often fail to attain their full growth, owing to this disturbance at the growing point, and as a result of the yielding nature of the new tissue they are unfit to perform their functions properly, and they become bent by pressure or twisted out of shape by muscular action. If the periosteum of a long bone is the principal seat of the disease, the shaft of the bone becomes curved; if, however, the disturbance is greater in the epiphyseal line, there will be a crook at the end of the bone when pressure is brought to bear upon it. In consequence of these changes in the skeleton the subjects of rickets become not only deformed, but are often greatly stunted in their growth (Fig. 85).


FIG. 85.—Extreme Deformity of Skeleton due to Rickets, showing enlargement of the ends of the bones (Sp. 1545, Warren Museum).

The accompanying illustration (Fig. 85) is from a drawing of the skeleton of an Indian, twenty-one years of age, one of the Six Nations. His mode of locomotion was by a large wooden bowl in which he sat, and moved forward by advancing first one side of the bowl and then the other by means of his hands. The nodules or "adventitious joints" were "the result of imperfect ossification, or, in other words, of motion before ossification was completed."

The principal deformity of the head appears to consist in an enlargement of its transverse diameter, and there is a great prominence of the frontal and parietal bones. The head has the appearance of being unusally large, but careful measurements seem to show that this is due partly to its shape and partly to the imperfect development of other regions of the body. The fontanelles remain open an unusual length of time, and the parietal and occipital bones are often soft and yielding, giving to the touch a parchment-like sensation, due to the absorption of bone at certain points, while at others it remains very porous. This condition is known as *craniotabes.* The sutures also remain broad and soft and membranous. The bones of the face appear to be impeded in their growth, and they give, therefore, to the skull an appearance of unusual size. Dentition is in consequence retarded, and the teeth show an unusual tendency to caries. The upper incisors considerably overhang the lower. The very profound disturbance of nutrition which permeates the entire system is shown particularly in the changes found in the brain, which is often enlarged. More frequently, however, there is effusion into the ventricles, and as the result of this there is occasionally hydrocephalus as a complication of the disease. As a rule, these effusions come slowly, and they may eventually be absorbed. If they occur rapidly, they are often accompanied by convulsions, which may terminate fatally.

The earliest change seen in the thorax is a slight swelling of the sternal ends of the ribs or at the line between cartilage and bone. This row of protuberances, which is very characteristic of the disease, has often been called the "rachitic rosary." These swellings are caused partly by the growth between cartilage and bone and partly by periosteal growth. Deformities of the thorax are due to the pressure of the atmosphere on the thorax-wall, and to muscular action, and to the impairment of growth of the ribs. The circumference of the chest is small, and there is a sinking in of the ribs in respiration at the point of insertion of the diaphragm. Gradually the whole side of the chest becomes flattened. In this way the so-called "pigeon-breasted" deformity is produced. The clavicles are usually bent forward in a sharp curve, and the scapulæ may also be more or less distorted. The spinal column may be curved backward. Kyphosis is a very common deformity in this disease. Scoliosis and lordosis are also not unfrequently seen. The pelvis in moderately severe rickets is somewhat flattened; the sacrum sinks deeply into it, and the lower portion of the bone is bent sharply forward. The iliac bones are small and flaring.

If the pelvic bones are excessively softened, the promontory of the sacrum protrudes, the region of the acetabulum is pressed inward, and the symphysis becomes prominent, the deformity somewhat resembling that seen in osteomalacia.

Epiphyseal swellings are seen at the wrist- and ankle-joints, and in severe cases at the ends of the phalanges of the fingers and the toes. Where the shaft of the long bone is profoundly affected, not only deformity, but even fracture, may occur. The humerus and the femur appear to be the bones most liable to break under these circumstances.

In the graver forms of the disease there is usually a prodromal stage, during which a change seems to have taken place in the child's character. It no longer seems disposed to walk, and may not even be willing to leave its bed. Its temperament becomes irritable, and there is a great restlessness at night, with a tendency to throw off the bed-clothes. Some children have a tendency to bore their heads into their pillows, so that the scalp is often deprived of its hair. The appetite is capricious, and diarrhœa is not an infrequent accompaniment of an outbreak of the disease. There is loss of strength, and the skin becomes pale and is often bathed with perspiration, particularly about the head. A more or less well-marked febrile disturbance accompanies these symptoms, which may continue for two or three months.

When the changes in the bones have developed the appearance of the child is strikingly characteristic. The patient is diminutive for its age. The head is apparently large, the face small and pinched. The expression is intelligent, and the child is precocious rather than backward in its mental development. The muscles are soft and flabby, but there is no actual impairment of their movements. Although there is no genuine paralysis, reflex nervous disturbances are not uncommon. There is often great hyperæsthesia of the skin. Colicky pains in the abdomen are explained in this way, as are also attacks of laryngeal spasm, which is apt to accompany the hydrocephalic condition or inflammation of the air-passages.

The parts of the skeleton most likely to be affected first are the bones of the wrist and the ends of the ribs. Kyphosis is also a most common deformity, the curve being most frequent at the juncture of the dorsal and lumbar regions. The articulations are in general more or less relaxed. Later the other osseous deformities already mentioned occur.

In the lighter forms of the disease the constitutional disturbance may be very slight. Beyond a tendency to diarrhœa there may have been no disturbance whatever, and the first evidence of any disease may be the deformity in bone. In some cases the children appear to be in robust health. The disease in the bone may in this case be well marked: there may be found swelling of the ankles, the wrists, and the knees, and curved spine, narrow chest, and protuberant belly when the lower extremities are affected. The child assumes the rachitic attitude on standing. The thighs are straddled, the knees bent, the shoulders thrown back, and the belly prominent.

The disease is usually very slow in its progress, and it may last one or two years. In America the prognosis is rarely grave. In the severe cases death rarely occurs as a direct consequence of the disease, but rather as a result of the enfeebled condition combined with some complication. When the deformities are well marked they may remain permanently in a certain degree. Sometimes a spontaneous straightening of a curved limb may take place. Spontaneous arrest of the disease may occur at any stage.

The most effective prophylactic *treatment* consists in the proper feeding of children. The child should be kept at the breast as long as possible during the first year of its life. If the disease comes on during the nursing period, it may be necessary to resort to bottle-feeding or to careful attention to the condition of the mother's milk. In artificial feeding the rules of sterilization of food should be adhered to strictly if it is possible to carry them out. After six months the child may be given meat-juice or raw beef in small quantities.

Baths and friction of the skin have often a beneficial effect upon the circulation, and they are strongly recommended by Monti.

Cod-liver oil may be given in small doses even during the first year of life. Stimulants in small doses are also well borne in the very young, and they take the place of a tonic. Iron may be given to older children. The tincture of eucalyptus globulus in doses of from 10 to 40 minims, three or four times a day, is recommended by Stedman. The compound syrup of the hypophosphites and the syrup of the lactophosphate of lime are remedies which are frequently given.

Kassowitz, whose theory of the disease has already been referred to, recommends very small doses of phosphorus, and he regards this drug almost as a specific for the disease. He bases his view upon an experimental study of its effects upon animals. The disease being due, in his opinion, to an increased vascular action of the bone-forming tissues, he finds that phosphorus produces a decrease of vascularity and prevents an absorption of bone. Small doses of phosphorus were found by him to check the softening of the bone in a comparatively short time. These views are not, however, shared by other writers who have tried this drug. Bradford and Lovett find the syrup of the iodide of iron the most useful of the many drugs advocated in rickets.

3. Osteoporosis.

Osteoporosis, senile atrophy, and fragilitas ossium or osteopsathyrosis (ψάθυρος, fragile) are terms which denote closely-allied conditions of the bone. This change in the bone differs from that of rickets or that of osteomalacia in that there is simply an absorption of bone without the accompanying pathological change. It is effected by what is known as *lacunar absorption*. At the point where the absorption is to take place are found many nucleated cells or the so-called "osteoclasts," which appear to bring about a solution of the bony substance. They lie in an indentation in the bone called "Howship's lacunæ." These cells are quite numerous when absorption is taking place on a large scale, and they appear to eat into and give a rough appearance to the edge of the trabeculæ. In this way the medullary spaces become much enlarged, and the bone thus becomes more porous; hence the name *osteoporosis*. The medullary tissue loses its cells and appears to consist almost entirely of fatty tissue. This change may take place in advanced years in that condition known as *senile atrophy*. The change is seen in its most typical form in the flat bones, such as the bones of the cranium, the scapula, and the pelvis, and in those portions, more particularly, not covered by muscles. In the parietal bones the process may be so extensive as to cause destruction of the outer table and the diploë, and even of a portion of the inner table. Cases are reported where at certain points the entire thickness of the bone has been absorbed. The occipital bone is affected next in frequency, and lastly the frontal bone. Irregular depressions are formed on the surface of the skull by the unequal absorption at different points. There is also a formation of new bone to a certain extent, showing an effort at repair. Thus it may come about that there is a thickening in the diploë, and bony deposit may also be found on the inner surface of the cranial vault. The bones of the face may undergo a marked senile atrophy, and the alveolar processes may entirely disappear. In the spine and the bones of the extremities there is more or less absorption in the interior of the bone, the trabeculæ being much thinned and here and there being entirely absorbed. If a large portion of bony tissue thus disappears, the outer bone may sink in at this spot. If there is much external absorption, the bones become smaller, and this occurs oftenest at the articular extremities of the long bones.

When the absorption has reached a point where the strength of the bone has seriously been impaired, there is presented the condition known as *fragilitas ossium* (Ziegler).

There is seen in new-born infants a form of this fragility which appears to be due, according to Klebs, to disappearance or to imperfect development of the bone-forming cartilage. A section of the bone through the line of ossification shows the zone of growing cartilage to be very narrow. The bony trabeculæ growing up from beneath are very thin, and they contain only a few bone-corpuscles. Cross-sections in the shaft of the bone show that the medullary tissue has very few cells and has undergone gelatinous degeneration, and that the bony trabeculæ are permeated with an anastomosing network of canals in which here and there lie bone-corpuscles.

The movements of the fœtus when the bones are in this condition may be sufficient to produce numerous fractures, and in this way so many fractures may take place that the bones may extensively be comminuted. This atrophy of bone is often seen in the insane.

Among the symptoms of this affection are mentioned vague pains in the bones simulating rheumatism. There may be no sign whatever of the disease until a bone breaks suddenly from slight injury, as from muscular action. Lathrop reports the case of a woman eighty-two years of age who sustained a fracture of the right femur while she was standing at a bureau. For some time previous to the accident she had suffered severe pain at the point at which the fracture occurred.

Murray reports a case of a girl who sustained in all forty fractures. Many of the cases reported are, however, probably due to rickets or to osteomalacia. The main point of distinction between fragilitas ossium and these diseases is the brittleness of the bone, whereas in rachitis and osteomalacia, the lime-salts being largely absent, there is a tendency of the bones to bend rather than to break.

A frequent cause for lacunar absorption is the *inactivity of the bone*, which occurs when a limb or a part has been rendered useless and is unable to perform its functions. Thus the process is found going on in the bones of the stump of amputated limbs. In fractures that have healed with much displacement the overlapping ends become atrophied, and the trabeculæ in the interior of the bone, which played a part in supporting the weight of the body, disappear.

Neuro-paralytic atrophy of bone near the joints, or *arthropathy*, is caused by an absorption of bone associated with disease of the central nervous system. The absorption of bone is very extensive in such cases, and joints may thus become disorganized.

Atrophy may occur from pressure: this is seen in the bodies of the vertebræ which stand in the way of the expansion of an aneurism. A bone which becomes infiltrated by a malignant growth shows well the process of lacunar absorption. Here is seen the wormeaten-looking edge of the bone surrounding the disease lined with a single layer of osteoclasts (Ziegler).

4. Hyperplasia of Bone.

The formation of new bone occurs usually as the result of chronic inflammation. If the bone increases uniformly in size in all directions, the change is called "hyperostosis." If the bone becomes thicker and denser, the condition is described as "osteosclerosis." The growth of new bone may take place in the form of endochondral ossification—that is, at the junction of cartilage with bone—and in this case an increase in the length of the bone occurs. An increase in thickness is due to the periosteal growth of bone, and an increase in density is due to the apposition of new bone to the trabeculæ of spongy bone, and to consequent narrowing of the Haversian canals and the medullary spaces.

Among the most striking forms of this hypertrophy of bone are those whose etiology appears to be more or less obscure. The peculiarly deforming enlargements of the bones of the head and face were described as early as 1697 by Malphigi as "cranioscleroses." One of the most striking cases of this sort was reported in 1734 by Forcade. This surgeon had a son who was perfectly well until he had an attack of small-pox. As a sequel of this disease he suffered from a lachrymal abscess which suppurated for a long time. As a result of this abscess a growth about the size of an almond formed in the nasal process, which growth gradually increased until it obstructed the nasal passages and afterward extended to the upper jaw, the lower jaw, and the zygoma, involving the orbits with the exception of the cranial walls. Extensive exostoses formed on the bones at various points. The eyes were pushed out of their sockets and speech became difficult. The disease lasted over thirty years. At the autopsy the bones of the cranium were found to be much thickened and denser than normal.

Virchow has given to this affection the very appropriate name *leontiasis ossium*. Baumgarten and Millat independently made a study of leontiasis ossium, and they agree in regarding it as a disease distinct from all other types of bone-hypertrophy, such as acromegaly or ostitis deformans or the diffuse hyperostosis of syphilis. The disease begins in youth in healthy persons of both sexes; it is painless, and it starts most frequently in one zygoma. It consists in a growth, mostly symmetrical, of all or of several of the bones of the cranium and the face. The bony growth is at first porous, but later is sclerosed. The cranium is increased to several times its normal weight, and it becomes extremely hard. The disease brings about the most frightful deformity. Smell and sight gradually disappear, the eyes protrude, death finally occurring with symptoms of brain-pressure. The disease may last over thirty years, the other bones being unaffected. Virchow and Fischer report cases of hyperostosis of the sphenoid bone, and Virchow reports also cases of excessive bony growth of the frontal and parietal bones.

In some forms of the disease that have been operated upon it is a question whether sarcoma was not a complication. Such operations as have been performed give no permanent relief, and there appears to be no remedy for the disease.

Gruber describes a case which is interesting, as it suggests a possible connection between the growth of bone and erysipelas, a disease associated with those hypertrophies of the connective tissue seen in elephantiasis. A girl ten years of age suffered from an epileptic seizure, followed by pain in the head and delirium lasting for several months. An attack of erysipelas followed one of the convulsions. In her sixteenth year she lost her hearing and her head began to increase in size, the growth being accompanied by severe pain. She died a year later of a second attack of erysipelas. Virchow also quotes a case in which a thickening of the cranial bones was accompanied by an enlargement of the bones of the trunk and the lower extremities.

An example of this kind is described by Paget, who gave the name *ostitis deformans* to the disease. He first saw the case in 1856. The patient, a country gentleman forty-six years of age, had always enjoyed good health when, without assignable cause, he began to be subject to aching pains in the thighs and legs. The bones of the left leg began to increase in size, and a year or two later the left femur also enlarged considerably. These changes were followed, during a period of nearly twenty years, by a growth of other bones. The spine became curved and rigid and the head increased 5¼ inches in circumference. The bones of the face were not affected. The patient, when standing, had a peculiar bowed condition of the legs, with marked flexure at the knees. He finally died of osteosarcoma, which originated in the left radius. Paget collected eight cases, and it is interesting to note that in five of them death occurred from malignant disease.

The bones in the case just described were found after death to be very much thickened, and drawings of the femur and cranium show a marked osteosclerosis. In some cases of craniosclerosis the bone may become as dense as ivory. The appearance of this condition is shown in Fig. 86 (taken from a specimen in the Warren Museum), the history of which specimen is unknown.

FIG. 86.—Calvarium of a case of Ostitis Deformans (Specimen 1209, Warren Museum).

Taylor of New York reports a typical case of ostitis deformans, the patient being a Canadian. Cases have also been reported in the United States by McPhedran, McKenzie, and Gibney.

The bones most frequently affected are the tibia, the femur, the clavicle, the spine, and the cranium. There is no tendency to symmetry in the disease. According to Taylor, there appears to be a mixture of rarefying ostitis (osteoporosis) and formative ostitis (osteosclerosis). The femur and the tibia not only become thickened, but also become bowed under the pressure of the weight of the body, and the trochanters rise above Nélaton's line. The joints are not affected.

In forty-three cases analyzed by Thieberge, twenty-one were men and twenty-two were women. The disease appeared usually after forty. There was no history of heredity, syphilis, rheumatism, gout, or tuberculosis.

Acromegaly may be distinguished from ostitis deformans, as it is limited chiefly to hypertrophy of the hands, the feet, and the face. The spinal column is frequently enlarged, and there may be marked kyphosis. The head may also be enlarged, but the long bones of the extremities remain unaffected. In cretinism—for which it might be mistaken—the bones, as a rule, are shorter than normal, although the cranial and some of the other bones may become enlarged or thickened. In acromegaly there is true hypertrophy of the bone, and the disease begins at about the twenty-fifth year. There is a rapid pulse, and a tendency to palpitation and moderate muscular atrophy.

The so-called "giant growth of bones," or *gigantism*, is often congenital in character and is entirely unaccompanied with any inflammatory symptoms. It is often observed to develop after menstrual disturbances. A marked change takes place in the affected portion soon after birth. In one case reported by Fischer the amputation of an enlarged finger was followed by increase in size of the entire limb. The hyperostosis of the bones of these giant limbs is well marked, but there is nothing in their anatomical structure to suggest the presence of an inflammatory process. The disease differs from ostitis deformans in that the growth of bone is accompanied by equal hypertrophy of the surrounding parts.

Some writers believe that acromegaly arises in connection with disturbances of the pituitary body of the thymus gland. It is possible that both this disease and the giant growth may be connected in some way with disturbance of the nerve-centres. According to Putnam, acromegaly may be benefited by the employment of the thyroid juice or powder.

Fischer shows that an *increase in the length* of bone may even follow slight injuries. He reports the case of a boy twelve years of age who was run over by a wagon, causing a contusion of the bones of the right leg. In the course of a year this leg became 4½ cm. longer than the other, and the bones were also much thicker than normal. Taylor reports the case of a lady who fell, injuring the thigh without fracture. A gradual enlargement, with an outward curving of the bone, has since taken place. Fischer reports several cases of abnormal growth of the bone following necrosis. A case of shortening of 3¾ cm. after fracture was reduced to a shortening of 1 cm. by compensatory growth. Elongation of the bone is also mentioned as the result of inflammation of the joint.

In those cases in which there has been no suppuration the growth progresses slowly and suppuration never takes place. Where no distinct inflammatory process has preceded this growth it has been suggested that a chemical substance may be the cause of this change of nutrition. Ziegler calls attention to experiments which have been made by giving small doses of phosphorus and arsenic during the period of bone-growth, after which evidences of an increased formation of bone were found at the points of physiological activity.

The pathological changes seen in the *marrow of bones* deserve mention here. The marrow of children is bright red in color, which is caused by the presence of cells and blood-vessels. The stroma of this tissue is made up of a delicate network of branching cells, and the walls of the vessels to which its prolongations are attached are very thin. The cells supported in this reticulum are round, and they contain a bright nucleus and a nucleolus, some of the cells being vacuolated. They vary greatly in size. There are also cells containing eosinophile-granules, others containing fat-granules, nucleated and non-nucleated red blood-corpuscles, and pigment-cells, and also single and many-nucleated giant-cells. This tissue is supposed to play a part in the development of the blood, and it is probable that red blood-corpuscles are formed in it. These cells gradually disappear with increasing age in the long bones, and the stellate cells which form the reticulum change by the absorption of fat into fat-cells. After the age of from fourteen to sixteen years the marrow of the long bones consists principally of fatty tissue. In the flat bones the marrow retains its red lymphoid character. According to Tizzoni, the fatty marrow changes back to red marrow after extirpation of the spleen (Ziegler).

In old age the number of cells in the marrow decrease, and in their place a mucous fluid is found. The marrow appears to undergo a sort of gelatinous degeneration both at this period of life and in many chronic diseases. The amount of fat-marrow may occasionally greatly be increased. In many cases when the fat is absorbed lymphoid cells take its place. This condition is occasionally seen in leucocythæmia, in cancerous cachexia, and in chronic suppuration in bone. When the bone is injured hemorrhages often take place in the delicate vascular structure, particularly in the marrow of young individuals. This blood may be absorbed, leaving behind it pigment, or it may become the starting-point, when infected with pyogenic cocci, of osteomyelitis.

5. Phosphorus Necrosis.

Necrosis of the jaw, as the result of phosphorus-poisoning, was first noticed in 1838, soon after the introduction of the manufacture of phosphorus matches in factories. Of late years, owing to the introduction of the proper precautions in their manufacture, the disease has become much less common. This disease occurs almost exclusively among the operatives in match-factories. The chemical composition employed consists of phosphorus and chlorate of potassium, with particles of ground flint to assist friction, a coloring agent, and the best quality of Irish glue. The tipping of the match-sticks is accomplished by dipping their ends in a warm solution of the composition placed in hollow pans and maintained at the proper temperature by a steam-bath. From these dipping-pans fumes constantly rise into the faces of the workmen and dippers. Both in cutting the sticks and in packing the matches their hands, coming in contact with phosphorus, are sufficiently coated with the composition to appear luminous in the dark.

The regions chiefly affected are the jaw-bones, but the inflammation may spread to the adjoining bones and involve the vomer, the zygoma, the body of the sphenoid bone, and the basilar process of the occipital bone. How the phosphorus-fumes act upon the bones has been a subject of much discussion. By some it has been supposed that the arsenic which is often found with the phosphorus was the cause of the inflammation. Wegner has shown by experiment that the disease may be produced by the direct action of the phosphorus-fumes upon those portions of the bone on which the periosteum was exposed by dissecting off the mucous membrane. In confirmation of this view is cited the fact that those individuals who suffer from carious teeth are most liable to the disease. It is supposed that the fumes enter the carious cavity and reach the peridental membrane by way of the apical foramen (Potter).

According to Hirt, operatives with diseased teeth are affected three times as often as those with healthy teeth. Such individuals, therefore, are carefully excluded from some factories in America. It has been maintained, however, that the local inflammation is due to a general poisoning of the system, and the advocates of this theory point to the fact that many operatives work for several years in factories before being affected. Hutchinson mentions a case where the prolonged use of phosphorus internally led to typical necrosis of the jaw. Weak, anæmic, and tuberculous individuals are much more liable to be affected than are robust persons.

According to Mears, the statements made in regard to the introduction of the poison through carious teeth should be received with some modification. He saw numbers of operatives suffering from carious teeth who worked for years in match-factories without symptoms of poisoning. In all the cases of poisoning seen by him there was an accumulation of tartar around the necks of the teeth. In his opinion there is a chronic toxic condition of the system with local irritation of the gums, which may be aggravated by decayed teeth or by tartar. Under the influence of some exciting cause—as a cold—an inflammation may begin and extend to the periosteum. In many of the operatives complaining of ill-health from the fumes of phosphorus he noted hemorrhagic transudations from the gums. He believes that the poison is introduced into the system partly by inhalation and partly by being swallowed with the food, and that the toxic condition precedes the disease of the jaw. In some individuals these toxic symptoms are so acute, accompanied by nausea, vomiting, etc., that they are compelled to abandon work.

The inflammation begins probably in the peridental membrane, and spreads easily to the periosteum, with which it is continuous, and from this point works its way along, by a slowly-creeping inflammatory process, until a large portion of the covering of the bone may be involved.

The disease begins as an inflammation of the gum, accompanied by toothache. On removing the tooth a certain amount of pus is discharged from the alveolus and the inflammation extends to the alveolar process. One by one the teeth are lost in this way until the entire alveolar process may be denuded of its periosteum. A foul pus, with often an odor of phosphorus, is discharged from beneath the edges of the mucous membrane into the mouth. Meanwhile the external soft parts become reddened and very much swollen and indurated, causing much deformity and presenting to the touch the sensation as if an extensive and a very thick involucrum was forming. Dissection shows, according to Markoe, that new bone is not formed at so early a period. Pus may be discharged externally through several openings. In the interior of the mouth the swelling may so extend as to involve the tongue. By this time the whole bone becomes involved in the inflammatory process, and there occurs osteomyelitis as well as periostitis, with the inevitable result of necrosis. When the periosteum first becomes inflamed new bone is formed here and there on its inner layer, and after suppuration has separated it from the bone, these bony masses may remain adherent to the periosteum and form new bone, or they may be broken down and discharged. The most extensive bone-formation is found at those points where the periosteum has remained longest in contact with the bone, this being at its inferior border (Busch). In very acute cases when the periosteum is separated quickly there is a very small amount of new bone formed. The sequestrum can usually be removed through the mouth, as the alveolar portion of the bone is the part first exposed.

The progress of the disease is rarely so extensive on the upper jaw, as the free drainage of pus prevents the same amount of burrowing that occurs in the lower jaw. The upper maxilla is affected somewhat less frequently than the lower.

In consequence of exposure of the sequestrum to the cavity of the mouth the pus with which it is surrounded is mixed with saliva and undergoes decomposition, and the discharge from the mouth is sometimes of the foulest description. A portion of this material is inevitably swallowed, and accordingly the health and digestion of the patient suffer. The progress of the disease is slow, and toward the end the general health may greatly be impaired.

With the removal of the sequestrum suppuration soon ceases and cicatrization takes place. In the majority of cases a cure is finally obtained, but when the inflammation once begins it cannot be arrested until it has produced extensive destruction of bone. In those cases that terminate fatally death may occur from an extension of the process, in the way already mentioned, to the base of the brain, and from meningitis. The long-continued suppuration may lead to amyloid degeneration of the internal organs. In a certain number of cases pulmonary consumption may become a complication of the disease.

Much can be done in the way of prophylactic *treatment* by proper ventilation of factories. In some factories exhaust fans are so arranged as to remove the fumes promptly from over the dipping-machines. Careful washing of the hands before eating is a rule that should always be laid down. Individuals with carious teeth or in feeble health should not be accepted as operatives. According to Busch, the employment of white phosphorus should be abandoned, and amorphous red phosphorus, such as is used in the preparation of Swedish matches, should be substituted. The chief objection to this change is said to be the expense. Mears recommends the use of turpentine inhalations, basing his views upon the power of the vapor of turpentine to neutralize that of phosphorus. In many factories the operatives are in the habit of carrying wide-mouthed bottles containing turpentine, suspended by straps around the neck. In the early stages of the disease the condition of the teeth and gums should carefully be attended to, and any tendency to suppuration should be arrested by the use of gargles containing boracic acid, phenyl, myrrh, or alcohol. A weak solution of permanganate of potash may also be used to advantage.

When suppurative periostitis is established every effort should be made to limit the extent of the suppuration as much as possible. The periosteum should freely be incised and thorough drainage be given to the pus. The sinuses should be syringed out with a weak solution of carbolic acid or of corrosive sublimate, and the strength of the patient should carefully be maintained. There is little hope of preventing necrosis when once this stage of the disease is reached.

The question as to when the diseased bone should be removed is one about which many operators differ. The general weight of opinion at the present time is to wait until the sequestrum has separated, and until the new bone formed by the periosteum is sufficiently strong to preserve the shape of the original bone. The sequestrum should be removed through the mouth, as it is here freely exposed, and the deformity of the external incision will thus be avoided. Care should be taken to disengage the laminæ of new bone from the sequestrum, so as to injure them as little as possible during the operation of removal. After removing the dead bone the cavity may be dressed by a packing of iodoform gauze.

6. Arthritis Deformans.

Arthritis deformans is a chronic inflammation of the joint in which not only the joint-capsule, but also the bone, is affected in a way which may cause great deformity, but the function of the joint is more or less preserved. Many joints may simultaneously be affected.

The disease has received a variety of names, which fact alone seems to indicate that the pathology of the affection has not been understood. These names are—chronic rheumatic arthritis, rheumatic gout, arthrite sèsche, etc.

The *etiology* of this affection is obscure. It may occur in young people, but it is oftener seen in those past middle life. In aged people it is often accompanied by other senile affections, such as atheroma and ossification of tendons or of muscles. In some cases there appears to be a distinctly traumatic origin, as the disease is seen to follow injuries or fractures which involve the joint. Such conditions are not infrequently seen in the knee and the elbow, and occasionally also in the hips.

It may occur spontaneously in almost any of the joints, although it is most frequently seen in the finger-joints and the hip, but it is seen also in the shoulder and in the vertebræ. It occurs in all sorts and conditions of life and in all countries. There are few families in which there is not some aged member more or less afflicted with this frequent accompaniment of old age. Men are somewhat less liable to it than women.

There are two principal forms of this form of joint-inflammation—the *mono-articular* and the *poly-articular*. The former is found principally in the knee- and hip-joints (malum coxæ senile). The latter occurs in several joints at a time, attacking the fingers and toes, principally in women.

One of the most striking features of this affection is the change which takes place in the cartilage. This change consists in a breaking up of the surface of the cartilage into fine filaments, owing to the absorption of the cement-substance which holds the fibrillæ together. In a cross-section of cartilage undergoing this change there is seen an anastomosing system of lines and clefts, in some of which are seen cartilage-cells either in a state of proliferation or of degeneration. In a vertical section the cells in the deeper layers of the cartilage are seen in active proliferation. This cell-growth may be sufficient to produce thickening, and even nodules of cartilage, at certain points. In the deeper layers are also seen nodules of softening, and at other points is seen a growth of blood-vessels which have pushed their way up from the marrow of the bone. In this way the cartilage gradually becomes softened down, and is worn away by the friction of the articular surfaces, and the surface of the bone thus becomes exposed. At other points


FIG. 87.—Arthritis deformans, with Eburnation of Bone due to Absorption of Cartilage.

the bone undergoes the change which has already been studied as osteosclerosis. It becomes dense and receives, through friction, an ivory polish or *eburnation* (Fig. 87). In the poly-articular form there is often a pannus-like growth of the synovial membrane over the cartilage. This membrane becomes rich in cells and blood-vessels pushing their way into the cartilage, which softens and breaks down before this growth. Deep depressions are thus formed which subsequently run together. In such cartilage very large stellate cells with extensive proliferation are seen occupying large cavities in the bone, the exact nature of which cells is not clear. By some they are supposed to be chondroclasts (Weichselbaum). This growth of the synovial membrane may sometimes extend to the opposite side of the joint, and adhesions may be formed in this way.

In the bone changes of different kinds are going on. On the exposed surfaces is the eburnation already alluded to, and around the edges of the joint is exuberant hyperostosis, by means of which new formation of bone takes place, giving a peculiar shape to the articular end of the bone. In the interior the spongy bone undergoes absorption. Many of the trabeculæ disappear. There is rarefying ostitis which results in osteoporosis. As the result of these several changes the head of the bone appears as if it had at one time been composed of a substance capable of softening from heat, and while in that condition had been held carelessly while it was allowed to cool. The neck of the femur is bent at a sharper angle to the shaft. Around the head of the femur a deep fringe of bone overhangs the neck. The head of the bone is much enlarged or it is partially absorbed. The "molten" fringes of bone are seen at the knee- and elbow-joints: they overhang the bodies of the vertebræ and often weld them to one another.

It should not be understood that the bone at any time is softer to the touch than the normal bone. On the contrary, the bone on the surface usually appears dense and even highly polished. Meanwhile, the tissue of the synovial membrane has been growing steadily. There is an increased production of connective tissue and blood-vessels, and frequently there is an excessive growth of adipose tissue. The capsular ligament and the synovial membrane become in this way much thickened. The folds of the joint and the villi become enlarged, and they grow into the articular cavity. These villi may become very numerous, and a joint thus changed may appear, when opened, to be lined with a furry membrane. Sometimes these elongated tufts may attain an unusual size, and occasionally they consist principally of adipose tissue, and the name *lipoma arborescens* has been given to these tumor-like formations. According to Sokoloff, these growths are due to the existence of a negative pressure in certain portions of the capsule, and are an indication that that portion of the joint in which they are found has been deprived of its function. At the point of the insertion of the capsule into the bone there may be bony growths of this shape which may become partially separated and attached only by a loose pedicle. Many of these outgrowths may finally become separated, and may collect in large numbers in the interior of the joint.

As a rule, there is no effusion of the joint-serum. Probably the function of the synovial membrane is materially altered, so that it produces less of its natural secretion. These chronic inflammations are therefore characterized by an unusual dryness of the articular surface. Hence the name "chronic dry arthritis."

The medullary tissue may undergo considerable degeneration, and may change to a gelatinous tissue, which may soften down, when extensive, and give rise to the formation of cysts. A lymphoid tissue may form in other cases.

The earliest *symptom* perceived by the patient is the presence in one of the joints of a certain amount of stiffness, which is increased with rest and disappears somewhat with exercise. Gradually the joint—as, for instance, the knee—becomes somewhat enlarged. This, however, is no symptom of inflammation, and on examination the increased size is seen to be due to an enlargement of the ends of the bones, and not to an effusion into the joint. Occasional attacks of pain, which are mistaken for rheumatism, are followed by increased loss of function, and this condition may be maintained without much change through a long series of years. The limb becomes considerably crippled, and the patient is obliged finally to use a cane or a crutch. This impairment of function is due to weakness of the muscles with partial stiffness of the joint, so that the limb cannot fully be straightened. The general health of the patient, however, is good.

The poly-articular form occurs usually in younger subjects. The joints, the hands, and the feet may suffer, as well as the larger joints. There are frequent exacerbations of inflammations after catching cold, at which time the joints become stiffer. Motion is also impaired by muscular contraction, so that certain limbs eventually become quite helpless. The deformity of the joint is not only great, but the bones are displaced upon one another by the contraction which takes place, so that in some cases complete dislocation may result. The general health remains good through a series of years, but in the most aggravated forms of the disease there may be great emaciation and enervation of the system, and the patient may succumb to some intercurrent acute disease. The disease in itself, however, is not fatal.

The *diagnosis* of arthritis deformans can be made partly from the history of the case, which will enable the surgeon to exclude gout or rheumatism, and partly from the local examination of the joint. The absence of fluctuation will also exclude dropsy of the joint. Old dislocations caused by the affection may be difficult to recognize from traumatic dislocation.

The *treatment* of this disease is usually most unsatisfactory, and patients are apt to wander from one physician to another and from one watering-place to another in search of a panacea. A great deal may be accomplished by an intelligent person in the management of his daily life, so that all disturbing influences may be reduced to a minimum. Iodide of potassium, the alkalies, and other rheumatic remedies should faithfully be tried. The use of hot baths at certain watering-places at the appropriate season, if carried out systematically at intervals during a series of years, may prevent the increase of the disease. Delicate patients should, however, resort to this treatment only under the most favorable conditions. Massage is a mode of treatment that will probably give more relief than any other.

7. Spinal Arthropathy.

Very extensive organic changes are found in the joints of individuals affected with disease of the spinal cord. Among those diseases may be mentioned tabes dorsalis, myelitis, laceration of the cord, and degeneration due to compression. These changes are also seen after nerve-section (Ziegler). The joints most frequently affected are the knee, the hip, the shoulder, and the elbow. The wrist and the joints of the fingers and toes are less frequently affected. Inflammatory thickening and ulceration are seen in the synovial membrane. Effusion takes place at the joint, and there is a swelling of the periarticular tissues. In the severest forms of the disease the capsule is entirely destroyed, and the ends of the bones undergo degenerative and formative changes. The articular end of the bone is absorbed, and a shapeless mass of bony nodules is left upon the end of the shaft of the bone. Suppuration only takes place in case the joint has been subjected to injury.

With the destruction of the articular ends of the bone dislocation usually takes place. The disease, which is supposed to be caused by an injury to the trophic nerves, is classed by many as tropho-neurosis. The origin of the disease has had but little light thrown upon it. The process is a chronic one, but it is frequently followed by a disability of the joint.

Excision has been performed successfully on one or two occasions, but it is probable that such treatment is indicated only in exceptional cases.

8. Ankylosis.

Ankylosis is usually divided into two varieties—*true* and *false*. True ankylosis formerly meant complete bony union of the two bones forming the joint, and it was confined to that variety. False ankylosis was a term used to denote stiffness of the joint due to contraction of the structures external to the joint, which prevented motion. Many writers reject the term "false ankylosis," and use the word "contractions" instead. The word "ankylosis" is, however, so extensively used to denote a stiff joint that it does not seem advisable to discard "false ankylosis." True ankylosis should, however, be used to denote the firm adhesion of one bone to another, whether it be by bone, cartilage, or by connective tissue.

The causes which bring about this variety of ankylosis are of an inflammatory character. Among these causes may be mentioned suppurative synovitis, trauma, particularly fracture into the joint, and inflammation due to adjacent disease of the bone, as tuberculosis or primary tuberculosis of the joint, etc. The histological changes that occur consist in the formation of granulation tissue, which may develop from the synovial capsule in a pannus-like growth over the cartilage, and become adherent to it. The cartilage at the same time becomes degenerated, and it is converted into a soft mucous tissue into which the connective tissue forces its way. Later the cartilage itself is changed into connective tissue. The granulation tissue also attacks the cartilage of the opposing bone in a similar way; consequently fibrous ankylosis takes place. Such a fibrous growth may consist merely of a few bands adhering to opposing cartilage, the rest of the joint remaining unchanged, or it may involve the entire articular surface, which is thus obliterated. The cartilage may be penetrated from below by the tissue growing from the medullary canals of the bone, and granulation tissue may work its way into the joint through this route. When the mass of tissue lying between the ends of the bones is mainly cartilage, only a small portion consisting of connective tissue, there occurs cartilaginous ankylosis.

If the cartilage has been destroyed entirely by the growth from the capsule and the bone, the granulation tissue intervening between the bones may ossify and produce a bony ankylosis (Fig. 88). In some joints may be found a combination of fibrous,

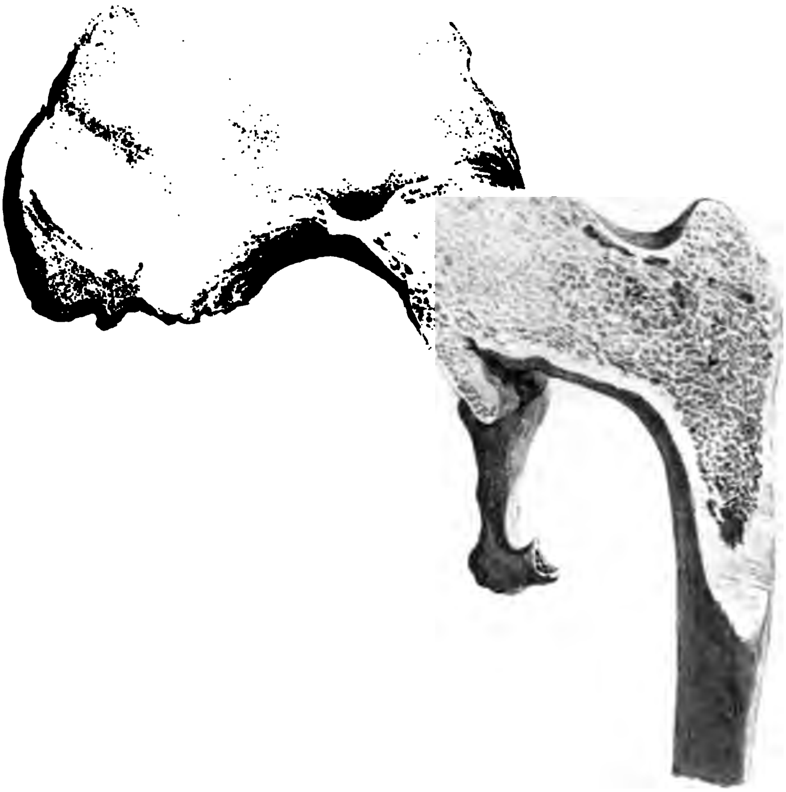

FIG. 88.—Ankylosis of the Hip-joint (Sp. 1421, Warren Museum).

cartilaginous, and bony union. In some cases the bony union is so complete that anatomical outlines are obliterated, and there is a continuous mass of spongy bone where the joint formerly existed. False ankylosis is due principally to conditions which exist in the capsule of the joint or to the parts external to the articulation. It is this form of ankylosis which is principally seen after fractures. The chief cause of joint-stiffness under these circumstances is, according to Bruns, cicatricial contraction of the muscles in consequence of injury received at the time of the fracture or from the shortening due to rest in the relaxed position. Contractions of the ligaments and fasciæ around the joints may occur in a similar manner. Menzel showed experimentally that the contraction of the fasciæ occurred quite early. Having placed the hind leg of a rabbit in a plaster bandage for eleven days, he found the stiffness of the knee-joint was immediately relieved by a division of the fascia lata. Adhesion of the tendons in their sheaths may also impair the motions of the joint. The stiffness and serous effusion which are found in joints near, and even at some distance from, fractures is almost a universal occurrence. Reyher sought to discover the cause of these pathological changes by experiments on animals.

Reyher experimented upon dogs with plaster bandages, keeping the joints confined during periods varying from ten to three hundred and forty-three days. Until sixty-two days had elapsed he found no change in the joint. After that time the first changes noticed were a shortening of the ligaments and of the capsule at those points that were approximated during the enforced rest. Later the capsule was found considerably thickened by fusion with the indurated tissue which surrounded it. The synovial membrane, however, remained normal. There was no sign of inflammation. In joints that had remained immobilized for a year those portions of the joint-cartilages which were actually in contact remained unchanged, while the portions that were not in contact had undergone degenerative changes. It was thus apparent that those portions of the joint which remained functionless during this period underwent fatty degeneration.

It is evident that we have here to deal with a degenerative rather than an inflammatory change. The joint has grown smaller, so as to accommodate itself to its restricted function. This does not account for the inflammatory changes, such as effusion and tenderness, which are seen in joints soon after using them for the first time. This point was also tested experimentally by Reyher.

Stiff bandages were applied on dogs for different periods of time, and after removing the bandages and applying passive motion the joints were opened and examined. In those joints which had been in the plaster for a few days no change was found. After an interval of thirty days there was discoloration of the synovial fluid and infiltration of the periarticular tissue. After one hundred and thirty-three days there was bloody effusion into the joint, eccyhmosis in the membrane, and rupture of adhesions.

These experiments show that true inflammatory changes follow the breaking up of the adhesion in the capsule, in consequence of which there is synovitis such as is ordinarily caused by a sprain. In the case of joints which lie close to the point of fracture there are signs of primary inflammation, which are often obscured by the principal injury. The joint may have been sprained at the time of the fracture, or the inflammatory process around the fracture may extend to and involve the joint. In such cases there may arise inflammatory changes inside the joint and conditions which may favor true ankylosis.

A knowledge of these various causes which produce stiffness in the joints will enable the surgeon to deal more intelligently with individual cases. In the use of passive motion care must be taken to confine it to those cases where inflammation does not exist, and to begin the movements so quietly as to cause as small amount of injury to contracted tissue as possible. Massage plays an important rôle in these conditions, enabling one to produce absorption of infiltration into the periarticular tissues, and thus to soften the part before violence is applied to it.

Where an articulation has been obliterated by a growth of whatever kind, and more or less of the cartilage is destroyed, the chances of restoring mobility by breaking up the adhesions between the bones are, as can readily be seen, exceedingly small.

When bony ankylosis has taken place resection of the joint may be performed in the upper extremity for the purpose of restoring motion. In the lower extremity this operation can only be employed for the purpose of straightening out a crooked limb.

9. PERIOSTITIS.

The periosteum is so intimately connected with bone that a consideration of this tissue as a separate organ is hardly advisable, and the behavior of periosteum in diseases of bone has already been referred to on several occasions in this book. There are, however, one or two affections of this structure which it is perhaps better to consider by themselves. In studying disease of the periosteum it is well to remember that this tissue is not only composed of the dense membrane which the dissector finds so difficult to remove from the bone, but also of an outer layer composed of connective tissue containing here and there a few fat-cells.

The inner layer is chiefly made up of fine elastic fibres forming a dense membranous network. In early life the periosteum is quite vascular, and is intimately connected with the epiphyseal cartilage, but much more loosely with the shaft of the bone. The blood-vessels contained in the periosteum make their way, usually at a right angle with the axis of the shaft, into the cortical bone, which is therefore to a certain extent dependent upon the periosteum for its nourishment. In case of extensive injury to this membrane the blood-supply may suddenly be cut off and necrosis or exfoliation of the bone may take place. The thickened periosteum which is found in cases of chronic periostitis is the result of an inflammation of the outer layer, chiefly of the periosteum.

Acute periostitis, particularly that form which terminates in suppuration, is usually secondary to some form of infective disease of the bone, such as osteomyelitis. It may also occur as one of the sequelæ of typhoid fever, scarlet fever, or measles. The non-suppurative acute type may be the result of trauma, and it is found principally upon the superficial bones, as the tibia.

The *symptoms* of an acute periostitis are those of a superficial swelling upon the bone, which is not thickened or enlarged. The swelling is exceedingly tender, the slightest pressure causing acute pain. The presence of pus is manifest by the redness of the skin and fluctuation in the centre of the inflamed mass. An incision will be followed by a flow of pus, and the appearance of the surface of the bone shows that that tissue has also been involved in the process, and is probably the primary seat of the inflammation. Usually the superficial forms of suppurative periostitis are not very extensive. The secondary suppurative periostitis which accompanies septic bone-inflammation may involve the greater portion of the shaft of the bone.

Many of the smaller subperiosteal abscesses are not due simply to the ordinary pyogenic cocci, but other organisms, whose pyogenic qualities are now recognized, are occasionally found. Park calls attention to a number of instances in which the typhoid bacilli have been found in periosteal inflammation, whether suppurative or non-suppurative, and he mentions a case in his practice of a boy who suffered a most intense and painful multiple periostitis during the end of the third week of an ordinary attack of enteric fever. Doubtless many such forms of periosteal infection are seen in other forms of infectious disease.

The chronic form of suppurative periostitis has already been described in connection with tubercular disease of the bone. It is rare to find a chronic suppuration of the periosteum which has not emanated from the bone beneath. In feeble and aged individuals an inflammation of the periosteum, due perhaps to a blow, may finally terminate in the formation of pus. Such abscess may contain either pyogenic or tubercular organisms. In some cases of inflammation of the periosteum of long bones, chiefly in young persons fifteen to twenty years of age, the solid constituents of the pus are comparatively few in number. Under these circumstances the contents of the abscess appear to consist chiefly of a mucous or synovial fluid. Such cases usually run their course without febrile disturbance. This form of periostitis has been regarded by Poncet and others of the French school as a type of inflammation which has not reached suppuration, but has formed an exudation rich in albumin. An attempt has been made to separate this variety as a special type of periosteal disease under the name *periostitis albuminosa*. It is not, however, recognized by Volkmann and others of his school. Vollert suggests that there may be a peculiar condition of the effused serum in which the pus-corpuscles are suspended, which causes the protoplasm to undergo a mucous degeneration, and thus brings about a destruction of the cells.

Chronic non-suppurative periostitis may occur as the result of injury, and a most obstinate and painful affection may be developed in this way. The result of such a form of periosteal inflammation is to produce not only a thickening of the periosteum, but also a formation of new bone, the result of the increased activity of the osteogenetic layers of the periosteum. The new bone forms very much in the same way as is observed in the development of callus. The bone appears much thickened at this point when examined at the bedside. A section through the bone, however, shows the shaft still well defined and of normal thickness, the new growth having formed entirely upon the surface of the bone. The bony trabeculæ forming around the blood-vessels and extending from the periosteum to the cortical bone run at right angles to those of the shaft of the bone, and the two layers are thus easily distinguished from each other.

It is this form of periostitis which is so often seen in the secondary stage of syphilis. In this disease enlargements may make their appearance upon the superficial bones, accompanied with symptoms of chronic inflammation. In addition to the new bone which is formed beneath the periosteum, there is a formation of bone around the trabeculæ of the old bone, in consequence of which a sclerosis or eburnation of the bone may take place. This osteosclerosis may eventually involve the whole thickness of the shaft of the bone, and the marrow may disappear. As this process may go on in different parts of the bone at the same time, great irregularities in the contour may result, and the surface appears very uneven. Such bones when macerated are very characteristic of syphilis. Occasionally the superficial bone-formation may amount to a growth of considerable size, resembling an exostosis. These bony growths are occasionally seen on the inner surface of the calvarium. Accompanying these bone-formations there is more or less pain, particularly at night, known as nocturnal and osteocopic pain.

In addition to the osteoplastic form of periostitis, there may be in syphilis suppurative periostitis. The swelling on the surface of the bone may become discolored and softened, and an incision will give vent to a small amount of thin pus. At the bottom of the pus-cavity the bone will be found eroded or carious, and a considerable amount of soft granulation tissue is seen in the interstices of the exposed bone. Surrounding the bone-ulceration there is at the same time a bone-formation, and after the abscess has healed a depressed cicatrix with a raised margin marks the site of the inflammatory process. If the suppuration is more extensive, there may be a destruction of a considerable portion of the bone beneath, and a sequestrum which has formed may eventually be removed from the bottom of the sinuses. Such sequestra are occasionally seen in the later stages of syphilis on the frontal bone.

Occasionally a prominent swelling may form on the surface of the bone, which swelling is at first hard, but later becomes soft, and when opened discharges a thick, clear fluid. The swelling, if thoroughly laid open, is found to consist of a soft and gelatinous tissue the result of degenerative changes. These gummata are found on the bones of the skull and the tibia, on the hard palate, and indeed on almost all other portions of the skeleton.

The destruction of bone produced by these forms of syphilitic inflammation may at times be quite extensive, and may be mistaken for tubercular or ordinary suppurative periostitis or osteomyelitis.

The *treatment* of periostitis in its chronic or non-suppurative form will depend somewhat upon the etiology of the particular case in hand. In the chronic non-suppurative forms, which are the commonest, the patient usually seeks relief from pain, which is chiefly felt at night, but it may also occur during the daytime. In many cases absolute rest in the recumbent posture is sufficient to give relief to the pain. The symptom is apt to recur, however, when the patient begins to walk again. Counter-irritation with tincture of iodine, blisters, or even leeches, will often give great relief. In obstinate cases, when local applications have failed to relieve pain, an incision should be made through the periosteum to the bone. In the tibia, where periostitis is so obstinate and painful, the incision should be vertical and of sufficient length to divide the thickened periosteum. The periosteum should then be slightly retracted, so as to relieve the pressure upon the bone, and the edges of the skin should be brought together so as to unite by first intention. In some cases it may be advisable to bore into the bone to determine the presence of an abscess. The surface of the bone should always be carefully inspected. In case of suppuration the surface of the pus-cavity should thoroughly be curetted, and the wound should be allowed to heal by granulation under a dressing of iodoform or aseptic gauze. In case of deep-seated suppuration in the bone with necrosis the abscess-cavity should be laid open thoroughly when the sequestrum has loosened, and the dead bone should be removed. The same radical measure should be adopted in the syphilitic cases of suppurative periostitis and ostitis that has already been laid down in the chapter on Osteomyelitis, and the internal administration of iodide of potassium, with or without mercury, should not be neglected. Many cases of chronic suppurative periostitis of syphilitic origin will heal rapidly without operation under specific treatment.

XXVIII. TUMORS.

THE word "tumor" is used freely by surgeons and pathologists to describe all kinds of swellings, but in its more limited significance it is applied to a certain well-defined group of pathological growths. A tumor may be defined as a malformation, non-inflammatory in character, existing as a more or less independent structure, not fulfilling any physiological purpose.

It was not until Virchow published in 1863 his work on tumors that there had been any scientific classification. Previous to that time all was confusion, and but few partially successful attempts had been made to substitute a more orderly arrangement. Many of the old names in use at that time show that surgeons were content to base their classification on the outward appearance or on the consistency of tumors. Some of these names, such as "fungus hæmatodes," etc., are unknown to the present generation, but such terms as "polyp" and "scirrhus" and "cauliflower" are legacies to which many still cling, and "sarcoma," still in good standing, was first used to indicate the fleshy appearance of certain growths.

Abernethy, however, during the latter part of the eighteenth century called attention to the resemblance which certain tumors had to certain tissues of the body.

There existed, however, among the laity, as well as among the profession at this time, a firm belief that tumors were a sort of parasite attached to and growing in the body. Many tumors were in fact classified as "entozoa." It was supposed that tumors were composed of structures essentially different from those which are found in the body, and that an independent circulation was formed in them, as in the embryo of the chick, and later a communication was established between its own vascular system and that of the body.

Bichat in attempting to divide tumors into two families—those which resembled anatomical structure and those which had a structure *sui generis*—showed himself to be influenced by the prevailing belief of the time. Lobstein introduced the words "homœoplastic" and "heteroplastic" to indicate this difference in growths. That he belonged to the school of humoral pathologists is shown by his assumption that tumors were formed from some sort of lymph. He recognized that the homœoplastic tumors were generally benign, and therefore he called the homœoplastic lymph "euplastic;" the other form of lymph he called "kakoplastic," to indicate that tumors formed from it were usually malignant in character. The latter class was supposed to develop from a dyscrasia which produced a profound change in the blood, and it was therefore hoped that there could be extracted from it a chemical substance which would represent its malignant quality—a sort of carcinomatin (which, by the way, has reappeared lately under the name of cancroin), and which would serve as a means of diagnosis. Tumors of all kinds were subjected to chemical examinations, and these views affected even so recent a writer as Rokitansky. A feeling, however, existed at that time that a more exact classification of tumors was needed. Fleischmann in 1815 declared that tumors were copies of the normal organic parts of the body from which they grew. John C. Warren, writing in 1834 on tumors, proposed "to present the different tumors under the head of the different textures of the body, so far as may be done." It was but a short time after this that Johannes Müller gave the law that "the tissue of which a tumor is composed has its type in the tissues of the animal body, either in the adult or in the embryonic condition."

The attempt to find a specific chemical substance having failed, an effort was next made to discover a specific sarcoma- or cancer-cell, and the view prevailed (more particularly in France) that the spindle-cell described by Lebert was the specific element of cancer.

It remained for Virchow to sweep away all theories about something specific, something which did not already exist in the body. He demonstrated for all time that cells could not develop *de novo* in a blastema or fluid, and that the type which rules in the growth and development of the body ruled also in the development and growth of tumors.

Tissues and cells may grow in parts of the body where they are not expected to be found, but they are always human cells and human tissue. It must not be expected to find plums or cherries, or even feathers, growing in the body, although hair and even teeth may be found growing where they do not belong. Virchow recognizes a homology and a heterology in tumor-growth, but not a heterology in the sense of Bichat. An isolated mass of epithelium growing in connective tissue or a cartilage-growth in the testicle are examples of heterology as found in the body of man. Tumors, however, cannot be classified under these two heads, for a certain growth may be homologous at one time and heterologous at another. As a rule, however, when a growth is found occurring in a tissue where it does not belong, it is probably malignant, and homologous growths are, as a rule, benign.

Of the various theories as to the origin of tumors, that of Cohnheim has of late years attracted most attention. This theory seeks an explanation in abnormal conditions of the embryonic cells. According to this theory there must have been in the embryo during its development more cells produced at some point than are necessary for the development of that particular region. This excessive cell-production may have been distributed over one of the germinal layers or it may have been limited to some one spot. In the latter case a single organ might be the seat of a growth at some future time; in the former, the whole system might be involved, such as the skin, the adipose tissue, or the bones. In confirmation of this theory Cohnheim quotes the experiments of Leopold, who showed that when fragments of cartilage from a young rabbit were transplanted into the peritoneal cavity they were more or less completely absorbed, but that when fœtal cartilage was used for transplantation there could be produced a considerable growth which might present the characteristics of an enchondroma. Indeed, Virchow called attention to fragments of cartilage in the shafts of bones near the epiphyseal line, which fragments might become the source of a tumor.

The occurrence of that variety of tumor known as "teratoma," as well as of many other congenital forms of tumor, is in favor of this theory. The dermoid cysts of the orbit and the neck are the results of an incomplete obliteration of the branchial clefts. That a child of ordinary size should sometimes grow to be a giant, or that gigantism of an extremity should develop after birth, is a possibility that can hardly be explained in any other way.

The embryonic nature of the tissues of sarcoma suggests the origin of these tumors from such remains of fœtal structure. The immediate cause of their growth, after a dormant period which may extend through the greater portion of life, is explained by Cohnheim as due to an increased blood-supply to the part. Physiologically, there is seen such an increased nutrition at different portions of the body at the age of puberty: with the development of the sexual organs there come a growth of hair and a change of features to those more closely resembling the parental type. At this time also the exostosis or the enchondroma may appear near the epiphyseal cartilage, and congenital wens may be noticed for the first time. It is well known that ovarian cysts or tumors of the breast are stimulated to increased growth at the period of pregnancy. Multiple fibromata and lipomata may readily be explained by the abnormal condition of the embryonic cells of a considerable portion of a germinal layer.

The growth of tumors in certain localities has been ascribed by Virchow to increased local irritation at those points. A familiar example is cancer of the lip, which has been supposed to be due to the use of the pipe. Cancers are frequently seen at other orifices, such as the pylorus, the os uteri, and the rectum. Cohnheim, however, explains this peculiarity by the complicated arrangement at these points of the germinal structures, where folds of the germinal membranes occur or where the germinal membranes join.

The hereditary predisposition to tumors is strongly marked in certain cases, and examples are not infrequent where cancer has apparently descended through several generations. In the family of a patient upon whom the writer operated for cancer of the breast there existed a marked hereditary predisposition. The maternal grandmother died of cancer of both breasts at the age of thirty; a maternal aunt died of cancer of the breast; a cousin on the mother's side died of cancer of the rectum; and an aunt on the father's side was operated upon the year before for cancer of the breast. Such family tendencies have been recorded, but they are not sufficiently numerous to establish a law. In 102 cases, 10 only were found by Lebert to have had ancestors who suffered from cancer, and Leroy d'Etiolles found only 1 such in 278 cases. A tendency to the development of malignant growths is supposed to consist in the inability of the surrounding tissue to resist. Thiersch seeks in this want of resistance in the connective tissue, brought about by age, an explanation of the growth of cancer at that period of life, the yielding tissue being unable to resist the growth of the epithelial structures.

Examples of the growths of tumors following injury are quite numerous. A lady applied to the writer for an opinion upon a lump in her breast. Four weeks before she slipped and received a blow at the spot from a gas-fixture. The swelling and discoloration caused by the blow subsided, but an induration remained. Eight weeks later the entire organ was infiltrated with carcinoma. Statistics collected by Boll in Langenbeck's clinic show, however, that in only 14 per cent. of the cases was trauma given as the cause of carcinoma, and Wolff's series yielded only 12 per cent. due apparently to the same cause.

Virchow divided tumors into three general groups: *histoid* growths, or those in which only one tissue is found, such as fibrous tissue, which is found in fibroma; *organoid* growths, or those which, like organs, are composed of a combination of tissues, such as epithelium and connective tissue, which, for example, are found in adenoma; *teratoid* growths, or those composed of one or more complex structures, such as hair, bone, and teeth, the commonest example of which is found in dermoid cysts of the ovary.

The classification generally adopted at the present time agrees with that which Virchow arranged on an anatomical basis. Several of the groups included by him in the family of tumors have been omitted by subsequent authors, such as the hæmatoma, the hygroma, the retention-cysts, and granulation tumors (tubercle, etc.).

Connective-tissue Group.

Fibroma,	Myxoma,	Glioma,	Lipoma,
Osteoma,	Enchondroma,	Sarcoma.	

Group of Tissues of Higher Function.

Myoma,	Neuroma,	Angioma,	Lymphangioma.

Epithelial Group.

Adenoma,	Carcinoma,	Endothelioma,
Cystoma,	Teratoma.	

Clinically, tumors may be divided into two principal families, the *benign* and the *malignant* growths. To the latter group belong carcinoma and sarcoma. A few of the other forms of tumors have occasionally malignant tendencies when departing from their usual type, but, as a rule, all other tumors may be regarded as benign.

XXIX. CARCINOMA.

Carcinoma may be defined as a tumor composed chiefly of epithelial cells, differing more or less in their type and arrangement from the normal epithelial structures and having a tendency to an unlimited growth. These cells grow into the surrounding connective tissue, which is thereby stimulated to increased development. Carcinoma is composed, therefore, of two distinct structures—the epithelial cells and the vascular stroma.

The epithelial cells, true so far to their type, lie in contact with one another, being more or less firmly united by a cement substance, or sometimes they are apparently continuous with one another, and are not supplied with blood-vessels. The stroma containing the vascular supply is arranged with alveoli, in which lie the cancer-cells. The absence of a tissue intervening between the cells is characteristic of epithelium, and it constitutes a mark by which, in doubtful cases, cancer is distinguished from sarcoma. In alveolar sarcoma is presented an arrangement of the cells closely resembling cancer, but close inspection shows that a fine reticulum of connective tissue separates the sarcomatous cells from one another.

Carcinoma (*καρκίνος*, a crab), or cancer, derives its name from the peculiar outward appearance which the disease has when infiltrating the skin, showing numerous prolongations, accompanied by hyperæmia of the blood-vessels. The word "cancer" has been used both by the laity and the profession to mean any kind of malignant growth: for this reason some pathologists prefer to discard the term. Its derivation, however, is the same as carcinoma, and it should therefore be used to signify only malignant epithelial growths, and be synonymous with carcinoma.

Cancer has its origin in the epithelial structure of the body only. Remak first formulated the law that the tissues of the embryo were developed from three germinal layers, and that the tissues of these layers were throughout life distinct from one another. This theory has not universally been accepted by pathologists, some of whom have thought that cancer might originate in connective-tissue structures. When it was discovered that cancer grew from endothelium as well as epithelium, this was supposed to be an exception to the law, but now it is known that these two kinds of cells spring from the same embryonic tissue.

Many pathologists have cited instances where cancer appeared to spring from bone or muscle, but in such cases it has generally been found that the primary growth was exceedingly small and had been overlooked.

The *etiology* of cancer, as has been seen, is still obscure, but a great deal of interest has been taken of late years in the question of the parasitic origin of this disease. The presence of bacteria in carcinomata has been noticed by numerous observers. Scheuerlen reported in 1887 a cancer bacillus which had been obtained by culture. The bacilli were short, and were capable of developing spores. These organisms, when inoculated into the mammary gland of bitches, produced tumors containing epithelial cells. Kubasoff injected into and fed to animals a bacillus he obtained from cancer, and it produced nodules in the internal organs. It was not clear, however, that these growths were epithelial in structure. Verneuil found certain bacteria in the degenerating parts of cancer that he thought stimulated the growth of tumors by exciting them to increased cell-production. Streptococci have been found in metastatic growths of cancer, showing that bacteria can be carried through the circulation to tumors, where they can settle and grow. Various forms of bacteria have been observed from time to time in carcinoma by careful investigators.

It is evident that these organisms form in cancer, and it is probable that they produce inflammations and necroses in the tumor, and in some cases, possibly, they have some connection with the cachexia, but no evidence has been adduced to induce the belief that they have any causal connection whatever with the tumor (Councilman).

The presence of intracellular organisms of quite a different character from bacteria has created much more speculation during the last few years.

Since the anatomical nature of cancer has been understood, it has been known that peculiar cell-like bodies are a characteristic feature of the disease. Some of these bodies are found in the so-called "epithelioma," and form the centre of cell-nests, and they were supposed to be cells undergoing degenerative changes, such as colloid degeneration or the horny change. In the alveoli of the more malignant forms of cancer cells apparently undergoing vacuolation are often seen.

Virchow as early as 1861 did not accept these views, but he suggested the idea of an endogenous cell-formation, and he named some of these cells "*physalides*" (φυσηλίς, a bladder). Recently the view has been gaining ground, although it is still strongly disputed by many good observers, that these cells existing within the epithelial cells do not belong to the human organism, but that they are animal parasites of a very simple organization, consisting of a single cell and classified as one of the numerous forms of *protozoa*.

A very brief account of the members of this family of the kingdom of the protozoa may here be given. The sporozoa were described by Balbiani as being composed of five different species of organisms—namely, gregarineum, coccidium, sarcosporidium, myxosporidium, and microsporidium. These parasites are widely distributed. They are found in all animals from man to the infusoria. Some of them give rise to epidemics of a grave character in animals, as the coccidium in the rabbit—quite a common disease in France, but rarely seen in America. The sarcosporidium gives rise to an epizoötic disease in sheep, swine, and poultry. A number of fish annually die of disease produced by the presence of the myxosporidium,[1] and the microsporidium is the organism which caused such ravages among the silkworms of France, producing the *maladie de la pébrine*.

The *coccidium* is the species said to be found in cancer, and is, therefore, of especial interest. This organism consists of a finely granular mass of protoplasm, with a nucleus not easily seen, and without an enveloping membrane during its period of growth, and in this period it inhabits an epithelial cell, where it becomes encysted. It finally breaks away from its host, and segmentation and sporulation take place. The spores may be voided from the intestine of an animal to enter that of another with the animal's food, and the cycle of development begins again. Sporulation may take place also inside the epithelial cell, as in the salamander, and during this process quite complicated structures form which it is hardly necessary to describe. The spores when freed enter a new cell, and thus multiply (Steinhaus). Balbiani was able to cultivate these organisms in water and in wet sand, and he was thus enabled to observe the changes which took place during sporulation. These organisms are very common in the livers of rabbits. Delapine found them in 92 per cent. of all rabbits examined. In

[1] Scott states that in American trout transplanted to New Zealand he has often found at the base of the tongue a tumor which proved on microscopic examination to be carcinoma.

the livers of these animals they form tumors, which are cyst-like, and appear to consist of a dilatation of the bile-ducts. These tumors contain epithelial tissue which is described as adenomatous and papillomatous. These organisms are found in the new-formed epithelial cells, and also occasionally one, or more, is found in giant-cells. There is considerable infiltration of the surrounding tissue with granulation cells.

That the pathogenic qualities of the sporozoa—or the "psorosperms," as French authors call them—are not confined to the lower animals has been recognized for many years. Gubler described as long ago as 1868 a tumor of the human liver that was supposed during life to be an hydatid cyst, but after death a large number of cancerous-looking tumors were found in the liver, one of them five inches in diameter. Within these tumors coccidia were found in or near the epithelium. There was very marked cachexia during life, as is so often seen in cancer. Podwyssozki found coccidia in cystic tumors of the bile-duct and in the liver-cells, causing irritation of the connective tissue and giving rise to icterus. He gave to them the name *karyophagus hominis*. They have also been found in the human intestine, accompanied by considerable destruction of the epithelium. They have been observed in cases where the epithelium does not appear to have been affected, as in pleuritic effusion and in the interstitial tissue of the kidney in a case of Bright's disease.

One of the first observations tending to associate these organisms with cancer was made upon a disease which was described simultaneously by Podwyssozki under the name of *psorospermose folliculaire végétante* and by White as *keratosis follicularis*. Darier attributed the disease to the presence of organisms resembling coccidia. He next studied them with Wickham in a case of Paget's disease of the nipple. In the mean time Thoma observed them in various forms of cancer. Darier describes them as enclosed in a hyaline membrane of double contour, from which they shrink when hardened in alcohol. These organisms as they grow push the nucleus into one corner of the cell which they occupy, so that it is often difficult to find the nucleus. Sometimes they are represented as consuming the nucleus; sometimes enclosed in a membrane, and sometimes without one. Sjöbring, who undertook to trace the cycle of development, followed them from the cells of a mammary cancer into the ducts of the gland, and finally he observed them in the stage of sporulation.

Russell reported that these organisms could be particularly well brought out by fuchsin staining, but he regards these fuchsin bodies as being closely related to the yeasts; Woodhead, who also studied them with fuchsin, regards them as coccidia. He found them most numerous in rapidly-growing cancers and in secondary nodules, and Metschnikoff, whose training qualifies him for determining the nature of such bodies, considers them parasites, probably belonging to the order of coccidia. The number of observations is now very great, and observers agree practically upon the morphology of these structures, such differences as are reported in description being probably due to accidents of growth in the tumor or to methods of preparation (Fig. 89).

There are one or two suggestive points brought out in this connection by different observers. Darier, in describing these organisms in cancer of the nipple, suggests that the corpuscles may have become implanted between the papillæ of the nipple during washing, as the coccidia live in water. The cultivation experiments of Balbiani in wet sand have already been alluded to. Haviland, who made a careful study of the geographical distribution of cancer in England, found that the disease is most prevalent in marshy regions and in the wet soil of river-basins subject to inundations. Woodhead points out that the conditions present in these localities are exactly those necessary for the development of psorosperms in rabbits—a disease which is most frequently met with among rabbits whose run is over marshy ground or over narrow areas where the drainage is imperfect.


FIG. 89.—Cell-inclusions in Cancer of the Breast, the so-called "protozoa" (oc. 3, obj. $\frac{1}{12}$ oil-im.).

Observers are not unanimous, however, as to the parasitic nature of these organisms. Schütz thinks that most of the questionable intercellular structures found in carcinomata should be regarded as due to leucocytes which have become imbedded in the cell. Klebs, after careful study and experiment, decides that there are no positive grounds for regarding these cells as parasites. He sees in the presence of these cells within the epithelial cells evidence apparently of the old French theory of the *action de présence*, the leucocytes exerting a fructifying influence upon the cancer-cells and causing them to multiply. Many still hold to the old idea that they are degenerated epithelial cells. All attempts to cultivate these cells from cancer-growth appear to have failed, and the number of cases in which cancer has been inoculated successfully into animals is exceedingly limited. Hanau succeeded in transferring a typical epithelium from a rat to two other rats. He succeeded also in transplanting an epithelioma from one part of a man to another portion of his body, and in obtaining metastatic deposits around the implanted growth. Cancer has been transferred from one locality to another in the same individual in several other cases. Wehr also successfully transferred cancer from man to dogs. Hanau does not, however, regard his experiment as proof of the infectious nature of cancer.

Councilman does not consider these structures parasitic, having seen them in many other morbid processes as well as in cancer. The parasitic origin he does not think has yet been proved, and on theoretical grounds it is hardly likely to be proved. Park, however, sees in these investigations sufficient to encourage the hope that surgeons are on the eve of great discoveries which will settle the question of the origin of cancer.

Cancer is said to be less common in tropical than in temperate climates. Haviland, as has been seen, proved the disease most prevalent in damp and in low-lying districts in England. It is said to be less frequently seen in Turkey, in Egypt, and in the West Indies, but this is doubted by Ziemssen. Negroes are generally supposed in America to be much less afflicted with cancer than the white race. In England statistics show that there are about 30,000 patients suffering at all times from cancer.

In the Tenth Census of the United States (1880) Billings states that the number of deaths during the census year was 13,068, of which 4875 were males and 8193 were females. He found also that cancer is most frequent among farmers, hotel- and restaurant-keepers, carpenters and joiners, physicians, clergymen, and sailors, while it is comparatively rare among printers, railroad officials, clerks, government officials, factory operatives, miners and iron- and steel-workers. An interesting map prepared by Billings shows that cancer is especially prevalent in the New England States and on the Southern Pacific coast; that it is prevalent in New York, Pennsylvania, and Ohio, in the interior of Michigan, and in the southern part of Wisconsin. It is least prevalent in the Mississippi Valley and in the South, and the proportions are generally lower in the coast regions than in the interior.

According to Park, the mortality from cancer is larger in and about Western New York and the adjoining region than in any part of the country save a limited area in California. Shattock has recently called attention to the fact that cancer, like tubercle, may repeatedly show itself in certain houses. This author reported a series of four cases of cancer occurring within fourteen years in persons unrelated by blood who were living in a single house. Power reports the history of three housekeepers who slept in succession for several years in the same bed-room. The first lived in the room for thirteen years and died of cancer of the stomach; the second after a residence of twenty years died of cancer of the liver; the third died at the end of eight years of cancer of the breast and uterus. They were all in good health at the time of their instalment in the position. Chapman reports a series of three successive unrelated occupants of a house who became affected with cancer of the rectum.

The cancer-cells, by their peculiar form, indicate their origin from epithelium. They are large cells of varying sizes and shapes, containing one or more round or oval nuclei with large, glistening nucleoli. They retain more or less the appearance and arrangement of the parent cells, so that the descendants of epidermic cells have the rough edges and a tendency to the horny change, and those which grow from cylinder epithelium have a tendency to remain cylindrical; but this is not always so, and in consequence of the rapid growth the cells are crowded into various shapes and they assume a polymorphous type. The departure from the anatomical type is so great at times that the new growth, although still epithelial, might with justice be regarded as a caricature of the normal cells.

The stroma, which is composed of fibrous tissue, is usually more or less infiltrated with small round cells. It may be abundant or scanty. When there are few epithelial cells the stroma makes up the greater part of the tumor, and there is a dense, hard growth, but when the epithelium appears to predominate the trabeculæ, which separate them into different clusters, are thin and the growth is soft. If the cut surface of a soft cancer be scraped with the sharp edge of a knife, there is obtained a milky fluid, the so-called *suc cancéreuse*, which was supposed to be a diagnostic sign of cancer, but which is merely the fluid and the pulpy tissues that contain the cells. There is nothing specific in the appearance of these cells. Usually there are several clusters of cells adherent to one another, which are suggestive of cancer, but a positive diagnosis can be made only with the microscope, when the epithelial cells are seen lying in their alveoli.

Cancer begins to grow by multiplication of the epithelial cells of the part. If the very first change seen in a cancer of the breast be studied, a proliferation of the epithelium of an acinus will be found, so that it becomes distended with the growth. The hyaline membrane of the tunica propria presently disappears, and later the outer layer. The epithelial growth now breaks through into the surrounding connective tissue and makes its way along the route of the lymphatics. The rapidity with which such a growth may take place depends largely upon the power of resistance of the surrounding tissues. The thin walls of a gland or a duct may yield readily, but the thick layer of the corium is much more resistant, and carcinoma in this region pursues, therefore, a much more chronic course.

The route through which cancer spreads to distant parts is through the lymphatic system. In this respect it differs from sarcoma, which spreads much more frequently through the blood-vessels. The cells are pushed forward chiefly by the pressure caused by their growth. It is possible that they may progress also in virtue of active movements that have been observed in them (Carmalt). The lymphatic glands are affected early in the disease.

In a case of cancer of the breast which the writer removed recently the patient was able to state the exact date of its origin, the place where the growth was formed having been examined a day or two before. The operation was performed when the growth was three weeks' old, and already a nodule the size of a small pea was found in a lymphatic gland of the axilla.

If such a gland be examined, at first the lymph-spaces will be found crowded with cancer-cells. The tissue of the gland is soon invaded, however, and it becomes plugged by the new growth, so that the disease is arrested for the moment at this particular point. Later the cells grow into the neighboring tissue and the process of infection continues. As the cancer spreads it becomes more vigorous in its growth, and during the later stages of the disease it destroys dense fascia and even bone. It progresses here by substituting its tissue for that of the organ which it invades. Occasionally it may be carried through the blood-vessels in an embolus to a distant organ. The internal organs that are most frequently the seat of metastatic deposits are the lungs and the liver. The secondary deposits are usually nodular in character, but occasionally there may be diffuse infiltration of an organ, as if the capillary vessels had been filled with an infective mass of cancer.

The secondary nodules, as a rule, show a strong resemblance in their structure to that of the original growth; even some of the degenerative changes seen in the primary growth may be repeated. Occasionally in rapidly-growing cancers the metastatic growths may depart from the original type, and in some cases the cell-growth is so active that the alveolar arrangement seems to be lost, and it is only by careful study that carcinomatous structure can be demonstrated. In such rapid forms of growth a general metastasis may take place, to all parts of the system probably, by multiple minute emboli. Such a condition is termed an *acute miliary carcinosis.*

The constitutional disturbance caused by the disease is known as the *cancerous cachexia*, and it consists in rapid emaciation, anæmia, and loss of strength. The growth of cancer is supposed to produce this condition in virtue of the injurious influence which it exerts upon the organs. It also abstracts material from the system for the nutrition of the growth. Rindfleisch assumes that the normal epithelial cells aid in the elimination of certain chemical substances from the system. When, however, these cells are enclosed in spaces in the interior of the tissues, as in cancer, the substances cannot be thrown off, and at the same time the products of the degenerative processes that are going on in the growth are carried into the circulation, and they exert a poisonous influence upon the blood.

The retrograde changes seen in cancerous growths show themselves often quite early. Cancer-cells are prone to undergo fatty degeneration, particularly those remote from the supply of nutriment. In this way the central portions of a nodule break down and a central depression is seen. In cancer of the skin ulceration takes place in virtue of these changes. Many forms of cancer undergo colloid degeneration, which involves frequently not only the cells, but also the stroma. As this change frequently occurs in the beginning of the disease, it gives a character to the growth that places it among the special forms of cancer to be noticed presently. Calcification is occasionally seen in cancers whose growth is feeble. As the carcinomatous tissue is an imperfectly organized one, and as the walls of the blood-vessels are softened by cell-growths, frequent hemorrhages and necroses occur, and considerable portions of the diseased mass break down and are absorbed.

The carcinomata are divided into certain groups according to differences which exist in the nature of the cells. Those cancers consisting of pavement epithelium constitute the variety to which the name *epithelioma* was given. This term, which was used before it was recognized that all cancers were epitheliomatous, was intended to represent a class of cancers that were less malignant in their type. The name is still retained, principally for this reason. "Epitheliomata" are situated upon the skin, but they may likewise be found upon the vagina and the cervix uteri and in the mouth and the œsophagus. Cylinder-cell carcinoma is composed of cells such as are found on intestinal mucous membranes. This form of cancer, which has a strong resemblance to glandular tissue, is therefore frequently called "adeno-carcinoma" or malignant adenoma. Carcinoma of the breast is characterized by the presence of a more globular type of epithelium. It is, however, chiefly in those cancers where the type of epithelium is very striking in its appearance that the cell-names are given, such as pavement- and cylinder-epithelial-cell carcinomas.

Cancers may be divided into several groups, according to their coarse appearances, which are due principally to the relative amount of cells and stroma of which they are composed. Thus, cancers of the breast, where they contain a large amount of epithelial cells arranged in a delicate alveolar stroma, are necessarily soft and juicy; consequently, they are known as *medullary cancers*. Those cancers containing an abundant dense stroma, in which a few small alveoli are found, have but few cells, and they are known as *scirrhous* or hard cancers. Carcinoma simplex is a name given to denote an intermediate stage of density, but this term is rarely used. The medullary forms are, as may be supposed, much more malignant than the scirrhous.

Colloid is a name given to those forms of cancer in which the cells have undergone colloid degeneration. This variety is found in various regions of the body, and the same type of cell does not always prevail.

The colloid cancer should not be considered as a special variety, but rather as a form of degeneration. The colloid material is deposited in the cells at first in small drops which run together, and eventually the whole cell is altered. The cells break down and many of them disappear, and the alveolus becomes distended. The tissue is very transparent, and, as little is seen but large alveoli formed by the absorption of many of the trabeculæ, this variety is sometimes called "alveolar cancer." There is some difference of opinion as to the origin of the colloid matter. Some think it is elaborated by the cell; others assume that it is exuded by the vessels; Müller suggests that it is developed first in the stroma. These cancers are seen principally in the stomach, the intestine, and the peritoneum; they are found, though rarely, also in the breast. The writer has seen a typical colloid-cylinder-cell cancer growing from the nasal mucous membrane. The development of colloid cancer is unusually slow. This peculiarity is attributed to the change in the cells, which interferes with the rapidity of its growth.

When the cells of a cancer are filled with granules of pigment there is presented a variety known as *melanotic carcinoma*, but this form is exceedingly rare.

"Endothelioma" is a name given to certain varieties of carcinoma by pathologists who wish to distinguish those forms that originate from endothelium from those forms which develop from epithelium. The cells of these tumors closely resemble those of epithelial cancers, and it is quite difficult to distinguish between them. They may often appear as pavement-cells or as cylinder-cells. A differential diagnosis can only be made in such cases when it is possible to determine the exact point of origin of the tumor. They are found in the skin, in the meninges, and in the serous cavities, where they are often seen as disseminated miliary nodules. This distinction is one rather of scientific than of practical interest.

A practical method of division of cancers is one based upon the localities in which they grow; therefore there will be described separately cancers of the skin, of the breast, of the uterus, of the mucous membranes, etc. These groups correspond pretty accurately to the different types of cancer-cells which have already been described, for the cells of a cancer resemble always the epithelial cells of the region in which they first appear.

1. Carcinoma of the Skin.

Cancers of the skin belong to that variety known as *epithelioma* or pavement-cell epithelioma. There are, however, two varieties of the disease, which may be distinguished not only by their histological, but also by their clinical, peculiarities. These varieties are, first, the superficial form, which is composed largely of a single type of small epithelial cell; and the deep-seated or polymorphous type, which is composed of large pavement-cells and of small epithelial cells. The superficial form, which is a far less malignant type of cancer, is found on the face principally, and is often known as a *rodent ulcer.* The deep-seated form is found on the lip, the penis, the scrotum, and the back of the hand, and, although much less malignant than other forms of cancer, is more frequently followed by infection of the lymphatic glands than the superficial variety.

The *deep-seated form* begins as a growth of cells from the epithelial layers of the skin, from the interpapillary space, and, according to some authorities, from the hair-follicles and the sebaceous glands. The first change usually noticed is an enlargement of the interpapillary masses of epithelium, which masses become elongated and grow down into the connective-tissue spaces of the cutis. They branch here in various directions and become constricted and distorted, and finally they are found in the deeper tissues of the skin separated from the epithelial layers above. The connective tissues in which they are now imbedded form a vascular stroma rich in cells. The cells of these epithelial clusters have more or less the characteristic peculiarities of the epidermic cells. A careful study of their shape shows that the outer layer is composed of a more or less perfectly formed epithelium, resembling the layer of cells found in contact with the papillæ of the skin. The cells nearer the centre are of the large pavement type, and in consequence of the rapid growth they are squeezed together and form concentric circles of cells, which are flattened out and undergo horny degeneration. In this way are formed the "epithelial pearls" or "cell-nests," as they are called (Fig. 90). If a fresh specimen of this form of cancer is cut open and the surface is slightly squeezed, there will be pressed out little comedo-like plugs which are composed of these epithelial nests.


FIG. 90.—Cell-nests in Cancer of the Lip (oc. 3, obj. D.).

In some of these epithelial pearls is occasionally found one of the so-called "psorosperm" bodies, appearing as a mass of nucleated protoplasm which has shrunk away from the surrounding cells, leaving a space or vacuole. There is seen in this type of cancer, growing luxuriantly, all the cells found in the normal epithelial layers of the skin. There is not only the small-cell, which is found in the deeper layers of the rete mucosum, but also the large pavement-cells, and even the horny cells of the epidermis. We have, then, a polymorphous type of epithelial growth. It is not always easy to see the points from which spring these masses of cancer-cells. Usually they spring from the deep layers of the rete. Many of the sections made show clusters of cells which appear to be altered and degenerated sebaceous glands. The transition changes, however, are not easy to observe, and the writer has been unable to trace such growths from the sebaceous glands, although most authorities agree that these glands are often the starting-point of the disease. It is an interesting fact that clinically there is seen considerable disturbance of the sebaceous glands in many cases of carcinoma cutis.

The *superficial form of cancer of the skin* is, as before noted, much less malignant, and there is found here a very different type of cell-growth. The cell-masses in most cases appear to grow down from the deep layers of the rete into the cutis vera in columnar masses which anastomose freely with one another. The epithelium is small and delicate, and it reminds one strongly of that seen in the rete mucosum near the borders of the papillæ or in the sheath of the hair-follicle. These columns of cells occasionally swell into large and irregular shapes, and there is found at certain points in such clusters a larger epithelium around which there is a concentric arrangement of cells; but these epidermic balls are extremely rare. In many cases the amount of epithelium is very small for cancer, and the stroma, which is composed of dense fibrous tissue, seems to make up the greater part of the growth. In such cases there is presented a delicate anastomosing network of columnar masses of cells, such as is described by the French writers as *epithéliome tubulé* (Fig. 91). It is claimed by Thiersch and others that this variety takes its origin from the sudoriparous glands, and by some writers it is known as *adenoma* of the sweat-glands. These cell-masses, whatever their shape or size, grow very slowly, and they remain for a long time confined to the upper layers of the skin. When the number of cells is very small and the stroma predominates, there is quite a dense, hard growth, and the name scirrhus cutis has sometimes been applied to this condition.

From what has been written it is evident that the cancer-cells spring from pre-existing epithelium: this is a fact which long

FIG. 91.—Tubular Epithelioma, from a case of Rodent Ulcer (oc. 6, obj. aa.).

since has fully been settled. It is learned also that as cancer grows its epithelial cells appropriate everything that comes in their path, and that bone, muscle, and nerve all seem to melt away before the active cell-growth. In some of the writer's early investigations it seemed, when one studied carefully the outer edge of a cancerous growth, that the spaces first filled with cells did not always contain epithelial cells, and that the clusters of round cells as one approached nearer the centre of the disease gradually became epithelial. This suggested that the round cells in some way had to do with the development of the cancer-cells. French writers speak of the action of the epithelium on the round cells as an "*action de présence*," the young cells becoming in this way impregnated and endowed with epithelial properties. However these appearances may be interpreted, the fact remains that in rapidly-growing carcinoma the round cell infiltration of the surrounding tissue is abundant and the cancer-cells present an appearance less typical of epithelium. This view is held also by Rindfleisch. Gussenbauer maintains that not only the endothelium of the capillaries, but also the muscular fibres from the media, form embryonic cells which develop into cancer-cells. Weil has also observed similar changes in striped muscular fibre (V. Ziemssen).

Carcinoma of the skin occurs most frequently between the ages of fifty-five and sixty. In 948 cases collected by V. Ziemssen, 739 were men and 209 were women.

The superficial form of cancer is almost invariably found on the face, and it has frequently been called "rodent ulcer." This term was used before the pathology of the disease had been recognized, and it describes one of its most striking clinical peculiarities. Cancer of the face—and it might also be said cancer of the skin in general—is apt to be accompanied by a peculiar condition of the epidermal structures known as *keratosis*.

This affection is characterized by the formation on the face and the back of the hands of scabs or crusts, which exist for a long time before any malignant disease manifests itself. At first they appear as scales, slightly elevated above the skin surface and of somewhat darker color than the surrounding skin. The surface of the spots is sometimes shining and smooth, and is sometimes dry and covered with minute lightly-adherent scales. The spots are without sensation and attract little attention at first. Gradually they become more noticeable by increase in elevation and in depth of color, but their development is very slow, and years may pass before they attain sufficient growth to become troublesome. Eventually they present elevations, one-eighth of an inch above the general surface, consisting of dry, horn-like scales, which vary in color from the faintest yellow to the deepest black, and which may be removed with little violence by the nail, leaving exposed a superficial excoriation, either smooth or exhibiting minute conical elevations that are enlarged sebaceous glands (White).

Microscopically, there is seen a great thickening of the upper horny layer of the skin, which thickening is continued downward into the ducts of the sebaceous glands, distending them and forming prominent protrusions. The sebaceous gland is not changed, but it is much distended by retained secretions which become mingled with the epidermic crusts. There is more or less cell-infiltration in the surrounding corium. The appearance of the complexion is often characteristic. There is a peculiar wax-like transparency of the temples and the upper part of the cheeks, and just beneath the surface of the skin can be seen the yellow sebaceous glands. The true skin is thin and is in a state of senile atrophy. At some one spot a crust has gradually become more prominent than elsewhere: this may be upon the side of the nose or be over the malar bone or on the temple. On picking off this crust it is now seen that there is beneath it a papule with a moist and somewhat ulcerated surface. On excising this papule it will be found that a downward growth of epithelium has taken place and that the development of the cancer has already begun. Schuchardt interprets the series of changes just described as the symptoms of a chronic inflammatory process which is, he thinks, highly favorable to the development of cancer. He failed, however, to find that the sebaceous glands were in any case the point of origin of the malignant growth.

The superficial carcinoma begins usually after middle life, is extremely slow in its progress, and, inasmuch as it does not cause pain, and sometimes not even itching, it is neglected for many years, and it is therefore often not seen by the surgeon until it has assumed large dimensions. When observed in the early stage of development it is found that the new formation has broken down in the centre and an ulcer has formed. The ulceration is not deep, and the surface is quite flat and is surrounded by a pearl-colored rim. The shape often closely resembles that of a horn waistcoat-button. Around the edge of the ulcer the skin appears in a healthy condition. The absence of inflammation in the diseased part is characteristic of cancer. There is no red and infiltrated skin, as is seen around tubercular or syphilitic ulcers. The pearl color of the rim is due to the presence of the epithelial cells, and it is characteristic of this form of cancer. When there is extensive breaking down of tissues and inflammatory complications the presence here and there of fragments of this pearly rim, perhaps made visible by the use of a hand lens, will enable the surgeon to recognize the disease under its disguise.

As the growth slowly advances its ulcerating character becomes more apparent: it may take years to double in size. Sometimes one portion of the rim will suddenly begin to grow out of all proportion to the other parts, and the ulcer is replaced or is masked, as it were, by a tumor. Usually, however, it continues to spread slowly, but is still as superficial as ever, and if the patient lives long enough it may cover large surfaces, involving the nose, the eyelids, the eye, and even the whole side of the face. To this formidable condition the term *noli-me-tangere* has appropriately been applied (Fig. 92). In the case of the patient whose portrait is here given (Fig. 92) there was no enlargement of the lymphatic glands. The same absence of glandular involvement was observed recently in another individual, in whom there was extensive ulceration. The disease had in this case originated in the scar of a gunshot wound received during the Civil War, and had destroyed the side of the nose, the eye, the ear, and the cheek, including the corresponding half of the upper and lower lips.


FIG. 92.—Noli-Me-Tangere.

The slight malignity of these ulcerating forms of cancer has been explained by the feeble reproductive power of the small epithelial cells, but it is more probable that there are other factors to be considered, such as the anatomical seat of the disease and, possibly, the nature of the parasite—if there be one—which caused it.

Carcinoma of the face does not always ulcerate. Occasionally, and not infrequently, the growth of epidermal cells is abundant, and there is also an active development of the stroma, so that there arises a nodular or papillary form of growth. These tumors may sometimes attain considerable size, reaching the dimensions of an English walnut. Such growths, which have been described by Hutchinson as a fungating form of rodent cancer, are found on the temple or near one of the lids. When such exuberant growths break down prematurely, there is formed a deep ulcer with raised edges, and this appearance Hutchinson named "crateriform" ulcer. Such growths, though formidable in appearance, are not liable to recurrence if they are so situated that they can radically be excised. One of the most important strategic points of cancer of the face is the region over the nasal process of the superior maxilla. A carcinoma originating here or gradually working its way toward the inner margin of the orbit may suddenly involve the lymphatic vessels leading to the base of the skull. When once the margin of the orbit has been passed the disease may be regarded as incurable.

There is a period in the life-history of this disease when the benign type may suddenly be changed to a malignant type, and a superficial cancer will then be transformed into the deep-seated variety. Irritating modes of treatment often rouse a sleeping cancer to frightful activity.

The deep-seated or polymorphous-cell cancer has its type in *cancer of the lip.* Here also the disease has been ascribed to chronic irritation, in this case the irritant being the constant use of tobacco.

Mason Warren reports 77 cases of cancer of the lower lip. It was ascertained that all but 7 were in the habit of smoking. In many cases the fact of a habit of smoking could not be ascertained, but the interesting feature of this series was the fact that 4 were women, 3 of whom were in the habit of using a pipe. The writer remembers having seen but one case of cancer of the lip in a woman, and she was in the habit of smoking. In this case the cancer was in the upper lip. So many smoke, however, who do not have cancer that it must remain doubtful whether such a cause predisposes to cancer.

According to Mason Warren, the disease is seen oftener on the left side of the lip than on the right; it may occur on the median line. Like other forms of carcinoma of the skin, it appears after middle life, and is commoner between the ages of sixty and seventy than at any other period; occasionally it is seen between the ages of thirty and forty, and in the latter case the disease is much more active. The point at which the disease begins is the junction of the mucous membrane with the skin, and it appears either as a small papule or as a flat crust which falls off only to re-form. It soon assumes the appearance of a superficial infiltration of the vermilion border of the lip, and it has a well-marked, though shallow, circular outline. When examined under the microscope at this period the disease is found to consist in a thickening of the epidermal border of the lip. The outer papillæ are thickened and elongated, and as the centre of the disease is approached the downward growth of the epithelial cells is well marked. The disease, however, is still very superficial. The large epithelial cells are seen here, and the number of epithelial pearls is very great. When allowed to pursue its course the disease may involve a greater portion of the lip, and even attack the bone. The central portion is then ulcerated, and the ulcer is surrounded by thick and overhanging edges. The next point of attack is the submaxillary gland of the side on which the disease lies. This point can be felt readily by standing behind the sitting patient and pressing the tips of the fingers against the inner margin of the jaw-bone. A small bullet-like nodule rolls between the bone and the finger. In the later stages of the disease the glands of the neck become enormously enlarged, and the patient dies slowly with symptoms of marked cachexia. Metastatic nodules may be found in the internal organs, but they are not common.

The *prognosis* of the disease is favorable if an operation is performed while the growth is superficial ; this is not always the case. The writer remembers a physician who applied for operation about three months after the first appearance of the disease. There was no return in the lip, but a gland under the jaw began to enlarge six months later, and the patient succumbed eighteen months after the first appearance of the disease.

The question of operation upon infected submaxillary glands is one about which there is much difference of opinion. When small and movable the glands should undoubtedly be extirpated by a very free and extensive dissection of the region in which they lie. Under these circumstances the prospect of a final cure may be looked forward to with some hope of success : it is, however, a grave complication of the disease. After operation patients frequently return in a few months very much alarmed about an induration of the cicatrix. Such cicatrices are not infrequently excised, and it is then found that there is nothing but cicatricial tissue. If let alone the induration will eventually disappear.

Cancer on the back of the hand is of the same type as cancer of the lip. It is associated usually with marked keratosis senilis. Although polymorphous, the cancer grows slowly at first, and a papule covered by a crust may exist for years before the patient seeks relief. Such growths are not infrequently multiple. The danger is that the glands at the elbow may suddenly become involved. In one patient who suffered from this affection the writer removed four or five such growths, not only from the hands, but also from the face. Axillary involvement eventually took place, and after seven or eight years' duration the disease finally terminated life by metastatic deposits in the liver. The writer has also seen cancer originate upon the palmar surface of the hand in a case of palmar psoriasis. This case likewise terminated fatally, notwithstanding amputation at the wrist.

Cancer of the penis occurs in about 1 per cent. of all cases of cancer. It is seen most frequently between the ages of forty and seventy years. It may occur on the preputial fold, but it is oftener seen on the glans. It can be distinguished without difficulty from chancre or a syphilitic condyloma by the history of the case, as the growth is very slow. It is said to appear at first as a small vesicle or a wart on the frenum, which vesicle increases in size and develops into a papillary growth. As it enlarges the centre breaks down and leaves an ulcerated surface. It may remain localized for a long time, the tunica albuginea appearing to offer considerable resistance to the growth, but eventually it attacks the body of the organ and infiltrates the lymphatic vessels and the glands in the groin. The glandular infection is said by Kaufmann to be more frequent than is generally supposed. In 48 cases, 40 were found to have this complication. The glands in the groin are the first involved, and usually those near the point of junction of the saphenous and femoral veins. Occasionally the glands in both groins are affected. Phimosis, accompanied with more or less balanitis, is seen frequently in this disease. Demarquay found in 59 cases, 42 in which there was phimosis. The writer remembers two such cases which were cured by operation. Metastases are occasionally found in the internal organs. The disease runs its course if untreated in from one to two years. Kaufmann found the average duration of life in 38 cases to be twenty-two months. If the disease comes into the surgeon's hands early, the prognosis is favorable for minor operations.

Carcinoma of the labia is of the same type as that of the penis. It appears usually on the inner surface of the labia majora, and it is first seen as a circular ulcer. It might be mistaken for a syphilitic lesion, were it not that there is an absence of inflammatory change and a history of slow growth. If allowed to follow its course, it may extend around the ostium vaginæ and destroy the clitoris. The mons veneris may be undermined by an extensive infiltration, and the vulva is then converted into one large foul, ulcerating surface. The glandular involvement comes late. The disease is more malignant than cancer of the lip. It generally runs its course, if untreated, in about two years. Butlin, in an analysis of 31 cases operated upon, places the percentage of cures—that is, of those who have passed the three-year limit—at 16. If the disease is operated upon before glandular enlargement occurs, the chance of a radical cure is good. Owing to delay while trying specific or local treatment this golden moment is often lost.

Cancer of the scrotum is also of the large- or polymorphous-cell type. It appears to be a disease almost exclusively confined to English chimney-sweeps; hence it has been called "chimney-sweep's cancer." It was supposed to have disappeared since the law has been enforced forbidding sweeps to ascend flues; Butlin's investigations, however, show that this is not the case. In the St. Bartholomew Hospital in the course of twenty years 39 patients were treated for cancer of the scrotum. In the Middlesex Hospital from 1867 to 1882 there were 20 cases of cancer of the scrotum under treatment. At the St. George Hospital 9 cases were treated from 1869 to 1878. The statistics of the Registrar General show that during a period of three years there were 23 deaths from cancer of the scrotum, penis, testis, or groin.

A careful investigation by Butlin of the various hospitals of Europe shows that the chimney-sweeps in Continental Europe do not suffer from this form of cancer: this immunity he attributes to the protective costume worn by them and to their personal cleanliness. In England, although chimney-climbing has been abandoned, no efforts were made to protect the body from the soot which falls in greater or lesser quantity upon the sweep. In the United States the disease is extremely rare. At the Boston City Hospital from 1881 to 1889 there occurred but 1 case of cancer of the scrotum. The writer remembers having seen but 1 case at the Massachusetts General Hospital, and that was thirty years ago.

The disease begins as a wart. Many such warts form on the scrotum and are known as "soot-warts." They may exist for years, and some sweeps are covered with such warts upon the scrotum without suffering from cancer. In the course of time, owing probably to some special irritation, one of the warts slowly grows larger, becomes more prominent, and at the same time becomes deeply fixed, and its centre ulcerates. The cancer spreads slowly along the scrotum, being confined to the skin. Occasionally it penetrates more deeply until it reaches the tunica vaginalis, and even the testicle, which may be laid bare and in time be destroyed. Before the days of anæsthesia the disease was said often to destroy everything from the anus to the pubes, leaving a foul sore against which no treatment availed.

Secondary infection of the glands of the groin may occur late in the disease. Metastatic deposits in the internal organs are not reported, probably because autopsies are rare (Butlin).

Tar and Paraffin Cancer of the Scrotum.—This disease was described almost simultaneously by Volkmann in Halle and Bell in Edinburgh. Ogston in 1871 had written on the local effects of crude paraffin. This disease occurs among the operatives in coal-tar and paraffin factories, who are obliged to be in contact with the products of the manufacture in a more or less liquid state. These products induce great irritation of the surfaces exposed, such as the skin of the forearms. The skin of the body is described as dry and parchment-like, somewhat resembling the irritation produced by carbolic acid. The ducts of the sebaceous glands are dilated, and in the ducts are seen dark, comedo-like plugs, and acne-pustules abound. There is considerable thickening of the epidermic layer, which is raised into little prominences on the extremities as well as on the scrotum. Sometimes there is a more distinctly scaly condition. In new operatives there is considerable infiltration of the skin at some points, and the part is red and shining and is tender to pressure. In old cases, after the first acute irritation subsides, the epidermic thickening increases gradually. Warty growths appear, and finally at one spot carcinoma develops. The series of changes is not unlike that seen in cancer of the lip.

A histological study of the irritated skin shows a growth of the lower layers of the epidermis and of the rete mucosum. The hair-follicles are frequently distended with masses of epidermic cells, and in the deep layers of the rete are found spots of brown pigment. Near the carcinomatous nodules the dividing-line between epidermis and the cutis becomes very irregular, and the interpapillary masses of cells are enlarged and irregular in shape. The skin shows also a small cell-infiltration. When the zone of the cancer is reached there are found enormous numbers of epidermic balls and a polymorphous-cell growth into the deep layers of the cutis. It is evident that we have to do here with a chronic irritation of the skin affecting its epithelial structures for a long time, producing at first hypertrophy of some of these structures, and finally a tendency to indefinite growth, as in cancer.

In the deep rugæ of the scrotum the soot- or tar-products remain untouched for long periods of time, and it is here that the disease most frequently shows itself. It is possible, as Butlin suggests, that certain areas possess physiological and chemical properties, which differ from those of other areas of the integument as decidedly as they do in their coarse appearance. It has been suggested by Butlin that the crude paraffin, the brown coal-tar, and the stone-coal soot have specifically irritating qualities which favor the development of cancer. It has also been suggested that tobacco-smoke and tobacco-juice bear the same relation to cancer of the lip that these substances do to cancer of the scrotum.

Xeroderma pigmentosum is a skin disease in which cancer is a frequent complication which appears in early life.

Cancer in Cicatrices.—Cancer has been associated with scars by writers ever since Alibert described keloid, which he confounded with cancer. Cancer appears long after the scar is originally acquired, and it is seen most frequently in individuals from forty-five to fifty years of age. Males are said to be more frequently afflicted than females. Cancer seems to develop preferably in those scars which have been subjected to long periods of irritation. Cancers are found, therefore, in cicatrices of the limbs that hamper movement; consequently they are subjected to undue tension, or they are found in the scars of ulcers or of old wounds or of fistulæ. Ulcers form and heal in the cicatrices many times before cancer develops. The greater part of a lifetime may pass in this condition, and finally the disease breaks out. Reid reports a case in which the disease appeared sixty-one years after the original injury.

The scars of ulcers on the lower extremity often exhibit this peculiarity. The disease in these cases is usually of a mild type. There may be present the polymorphous- as well as the small-cell type of cancer, but the growth of the cancer is almost always exceedingly slow, and there is a history not unlike that of rodent ulcer. These cases may, however, take on a more malignant action at any time. In such cases there is likely to be found involvement of the inguinal glands. In 128 cases reported by Rudolf Volkmann of cancer developing in scars of the extremities only 12 cases were known to have died of cancer.

In a case recently operated upon the writer found a large ulcer, with a peculiar fur-like surface, that had evidently developed from the scar of an old varicose ulcer. It had already involved the shaft of the tibia, but, as it had existed for many years and had caused no pain, it was only with the greatest difficulty that the patient was persuaded to allow amputation of the limb. It proved to be a large-cell epithelial growth. The writer has already referred to a most formidable case of rodent ulcer of the face that developed from a scar.

The treatment of cancer of the skin, as indeed of cancer in general, may be stated to consist in the removal not only of all apparent disease, but also in the excision of as broad a margin as possible of healthy tissue. In the case of cancer of the skin this treatment can be carried out more effectually than in any other portion of the body, and, inasmuch as glandular infection comes late in the disease, operation is more frequently followed by cure in this than in any other region.

Rodent ulcer is perhaps the mildest type of cancer known, and in its earliest stages it can be scraped away, the base of the wound being bored with a caustic or touched lightly with the fine point of a Paquelin cautery. If the papule or ulcer is situated where it can be excised, this operation should be performed, as the wound heals speedily and leaves an almost imperceptible scar; and one should train one's self to take as much tissue as possible in order that the cure may be permanent. This is one of the hardest habits for the surgeon to acquire, as economy of tissue appears to be urgent upon exposed places. Occasionally a small nodule situated upon the side of the nose, if not radically removed, will begin to grow with frightful rapidity. Cancer of the face can permanently be cured, even though it has returned several times after operation and has involved cartilage and bone. The writer recalls the case of a gentleman who allowed a cancer to grow on the left side of the nose until it involved the skin of that side and a portion of the skin of the right side. The disease returned three times after thorough scraping and burning with the actual cautery. Finally, the left half of the nose and the ascending process of the superior maxilla were excised, and the cavity thus left was covered by a flap taken from the forehead. The disease never returned after this operation. Beyond the use of the Paquelin cautery for exceedingly small growths, the writer has abandoned the use of caustics in the treatment of this affection, as the results of incomplete removal are occasionally most serious.

Cancer of the lip should be excised by a V-shaped incision, including at least one-quarter of an inch of healthy tissue on each side. There is no danger of taking away too much, as the lip is elastic and its suppleness is entirely restored even when very large portions have been removed. Careful examination should always be made to detect infected glands, and the patient should be warned to search for the appearance of any lump under the jaw. A very free dissection of the upper cervical triangle may even then give the patient a chance for his life.

Cancer of the penis, when operated upon early, is curable. The disease should be scraped away, and the base of the growth should be sliced off as one would pare a corn until healthy cavernous tissue is seen. In more advanced stages amputation should be performed, and the groin should carefully be searched for enlarged glands. Winiwarter reports 12 amputations, of which 5 remained permanently well; 1 died of the operation; 6 had recurrences, 3 of which were in the stump and 3 in the glands. If the glands are removed early, there is still hope of cure, as the progress of the disease is slow. The bad reputation of this form of cancer is undoubtedly due to many incomplete operations; the same may be said of cancer of the vulva. Time is frequently lost in determining the diagnosis and in using specific remedies.

The writer succeeded in prolonging life for several years by yearly operations on a case of advanced cancer of the vulva, so that at the present time there is no vulva. The meatus and ostium vaginæ, much narrowed, now open in the centre of a cicatrix. A few months ago the patient was seen in good condition.

The treatment of cancer of the scrotum is attended with good results if taken in the early stages. The rule of free excision holds good here.

In cancer of cicatrices the disease is generally found in the centre of a large scar. If this scar is situated on an extremity, there is an excellent chance of saving the patient by an amputation, as the glands in the groin are usually not infected, although they may be enlarged by inflammatory infiltration. If the scar is situated on the face or the trunk, the best that can be done is probably a thorough curetting followed by the actual cautery. In some cases it would be possible to excise the ulcer, the wound thus made being covered by Thiersch grafts.

The tendency at the present time of following up the operative treatment of cancer by a subsequent course of internal medication should be encouraged. In the case of cancer of the skin the bromide of arsenic or Fowler's solution may be tried in doses of 2 or 3 drops three times a day for months after the operation. Patients should be asked to report every three months during the following year for inspection.

2. Cancer of the Breast.

The breast is one of the most frequent seats of cancer. In a series of 7881 cases of cancer collected by Andrews the disease appeared in the breast 1232 times. This region comes third upon the list, following that of the uterus and the stomach. In the great majority of cases it occurs in the female breast, and in the male breast the disease is extremely rare, being seen in about 1 per cent. of the cases. In a collection of 110 cases of cancer of the breast made by Dietrich 3 occurred in males. The number of deaths from cancer of the breast reported in the United States in 1880 was 1387.

The period of life in which the disease is oftenest found is that immediately preceding the menopause. In an analysis of 1622 cases Gross found that the average age was 48.66 years. It may be said that from forty to fifty is the commonest decade in which the disease is likely to occur; it is next most frequently found in women between fifty and sixty years of age; the period from thirty to forty years comes next, and that ranging from sixty to seventy follows. There is but one case reported at the age of twenty-one, but Bryant states that he has seen cancer of the breast at an earlier age. The writer had one patient in whom the disease was first noticed when she was twenty-two years and three months old. It was a well-marked case of cancer, as shown by microscopic examination, and it recurred, after operation, the following year. Although the disease appears during the period of the *functional decline* of the organ, it is said that 80 per cent. of the cases are found among married women, and according to Bryant it appears to occur among women who are prolific to an extreme degree.

The question of *heredity* having already been discussed, it remains merely to add here that of 1164 cases analyzed by Gross, in only 55, or 4.72 per cent., of the cases could the disease be said to have been transmitted. *Traumatism*, according to some writers, has a direct influence on the development of carcinoma of the breast in about 13 per cent. of the cases. Cancer of the breast in the negro is extremely rare. The writer does not remember having seen a case.

As to the *locality* of the disease, it may be said that it occurs about as frequently in one breast as in the other. If a line be drawn vertically and one horizontally through the nipple, the breast will be divided into quadrants. If now a circle be drawn around the areola, the breast will be divided into five anatomical areas in which cancer may be found. The disease was found by Gross to be seated more frequently in the upper than in the lower hemisphere, and more frequently in the outer than the inner hemisphere. The most frequent locality was found to be the upper and outer quadrant, that nearest the axilla, while the region of the areola came next in order. In exceptional cases it develops in an accessory gland or lobule below the clavicle, near the sternum, or in the axilla, where it may be mistaken for disease originating in a lymphatic gland. Cancer constitutes about 80 per cent. of all tumors of the breast.

The *classification* of cancer of the breast varies considerably in different works. The simplest and most practical arrangement is a division of the various forms into two classes—namely, medullary, or soft and rapidly-growing carcinoma; and scirrhous, or the hard or less malignant type.

The cells of carcinoma of the breast are of a more or less globular type of epithelium. They are very irregular in shape and vary considerably in size. They are contained in alveoli, and are grouped together in no well-defined order, but fill the alveolus usually with a solid mass of cells which are directly in contact with one another. In the *medullary* form the alveoli are either large or numerous, and they vary according to the shape of the plugs of cells that accumulate in the stroma. These plugs are sometimes round or oval in shape, and at other times are long and narrow, and cancers in which one or the other form prevails have been called by Billroth "acinous" or tubular. The stroma is composed of connective-tissue fibres in which there is more or less round-cell infiltration. It is sometimes exceedingly small in amount, only a few fibres forming the trabeculæ which separate the different alveoli, and in such cases the cell-masses or plugs are very numerous. The larger the number of cells the softer the tissue, and the term *medullary* is therefore a most appropriate one to describe such a condition (Fig. 93). In the periphery of the tumor the tissue which immediately surrounds the cancerous growth is usually infiltrated extensively with small round-cells. The stroma is not always the same in character throughout the growth, for at certain points it may be abundant, and may form broad fibrous bands which separate the soft cellular portions from one another. This is the case in tumors of medium density, which are sometimes called "carcinoma simplex"—a term frequently used in books, but rarely employed by surgeons.

FIG. 93.—Medullary Carcinoma of the Breast (oc. 3, obj. D.).

In the *scirrhous* variety the stroma is a predominant feature of the new growth, and the cell-clusters are few in number and small in size. The latter are found scattered at greater or lesser distances from one another, and are enclosed in elongated and spindle-shaped alveoli. They are in rare instances found to undergo calcification. The fibrous stroma is very dense and scar-like at certain places, and the fibres often run together, forming broad semi-transparent bands of tissue, with a few pigment-granules scattered here and there, but with very few cells (Fig. 94). In the extreme type of this form of cancer the cell-clusters are sometimes quite difficult to find, and in the early days of the microscope this form was called a "connective-tissue cancer," as it was supposed that no epithelium existed in it. This type of scirrhus has been called "atrophying scirrhus;" the dense forms of cancer, being very slow in growth, are consequently much less malignant in character.

FIG. 94.—Scirrhous Cancer of Breast (oc. 3. obj. D.).

The coarse appearances of these two forms of cancer also differ markedly from each other. The cut surface of a medullary cancer has a grayish-red color in which grayish striæ are seen formed by the fibrous trabeculæ which support the soft juicy masses of cells. There is no well-defined border, as the growth appears to infiltrate the surrounding tissues. By scraping lightly such a surface an abundant cancer-juice is obtained upon the blade of a knife, the juice showing under the microscope epithelial cells of most irregular shapes, single or in clusters, and floating in a turbid serum. The scirrhous cancer when cut open shows a mass of scar-like tissue which has caught in its projecting bands of fibres portions of the lacteal ducts and of other structures pertaining to the breast, that are in a more or less advanced stage of atrophy.

An unusual form of cancer of the breast is *colloid* cancer. It is so rare that the writer remembers having seen but two specimens. The appearance of a microscopical section is very striking. The alveoli are large and the stroma is thin and transparent. The alveoli appear to be distended with a transparent gelatinous material having circular streaks in it, as if it recently had been stirred with a glass rod. There are very few cells; sometimes one or two remain adherent to the wall of the alveolus, but more frequently a cluster of cells are found near the centre undergoing degeneration.

An example of the earliest change found in the epithelial structure of the breast in the development of cancer is seen near the periphery of a growing carcinoma. Here is found a growth of the epithelium filling up and distending a gland acinus. The hyaline membrane of the tunica propria of the acinus presently disappears, and the cells break through the deeper layers of the tunic into the surrounding tissue, and they begin to grow in different directions in the lymph-spaces.

Let attention now be turned to the *clinical history* of cancer of the breast. The first symptom noticed by the patient is a hard lump in the breast. It is only accidentally found, as there has been no previous pain and no symptoms of constitutional disturbance of any kind. When a healthy woman between forty and fifty years of age presents herself with such a lump, the chances are strongly in favor of its being a malignant growth. The nodule is usually seated in the upper and outer quadrant or beneath the nipple. To the touch the nodule appears to be firm and ill-defined as to its borders. In some cases the nipple is retracted, and if the axilla be explored with the tips of the fingers, there will be found one or more glands firm and matted together that slip between the fingers and the ribs. Often there is no retraction of the nipple, but in many cases a careful inspection will show that the skin overlying the tissues is depressed slightly, forming a shallow dimple. This pitting of the skin and the retraction of the nipple are due to the shrinkage which has taken place in the breast-tissues in consequence of the destruction that has been brought about by the diseased growth. The lump in the breast slowly grows, and finally it becomes attached to the skin, which gradually becomes destroyed, so that there is found in the centre of a reddened and infiltrated lump an ulcer which gradually increases in size. In many cases the tumor forms without pain, but as the growth progresses there may be lancinating pains. Pain is not, however, an important symptom, as many women of middle age are apt to suffer from neuralgia of the breast, particularly at or near the menstrual period. In such cases the writer has noticed a slight fulness of the breast, and even an enlargement of the axillary glands. The condition is readily distinguished from cancer, however, as in such cases there is no tumor to be felt. The nodulated masses felt in a mammary gland should not be mistaken for a tumor, and the best way to determine definitely the presence of a new growth is to press the breast firmly against the thorax-wall with the palmar surface of three extended fingers.

The tumor develops not only forward, but also backward into the pectoral muscle and the retromammary connective tissue. Even though the muscle appears to be free, the delicate fascia is often affected. The muscle may eventually become adherent to the growth, and later it may be perforated, and the tumor then becomes fastened to the ribs. This condition is recognized by the immobility of the nodule. While growth in this direction is taking place, the surrounding skin occasionally appears also to have become affected, and numerous red nodules crop out in various directions. In this way a large area of the skin of the chest may become diseased, and there is presented the condition known by French writers as *cancer en cuirasse.* Occasionally the original tumor enlarges with frightful rapidity, and often with the appearance of an inflammation. The skin of the breast becomes reddened and slightly œdematous, showing a well-defined outline (Fig. 95). This redness spreads over the whole breast, which becomes hard and brawny, and the infiltration involves the skin of the thorax-wall beneath the axilla. Such fulminating cases are fortunately rare.

FIG. 95.—Brawny Infiltration of Breast in Cancer.

As the disease progresses in the mammary gland the *glands in the axilla* become enlarged and matted together, and they fill out the cavity of the axilla with a firm nodulated tumor. At this time there may be observed in the supraclavicular region a slight fulness which is not to be seen on the other side. This appearance shows that the axillary infection has spread beneath the clavicle. From this point the cancer-cells follow the chain of glands which accompany the internal mammary artery, or they may next infect the bronchial glands at the root of the lungs.

When the tumor is very near the sternum, Volkmann has seen the axillary glands of the opposite side also infected. It is stated by Billroth and Winiwarter that glands felt in the axilla and above the clavicle may in some cases disappear after operation. This disappearance can only be explained on the theory that they were inflammatory. In the case of inflamed cancers such enlarged glands might be found, but so far as the writer's experience goes such fortunate retrograde changes are not seen.

The infection of the lymphatic glands in the axillary and subclavian regions finally becomes so extensive that the return of the venous blood and lymph is retarded, and an œdematous enlargement of the arm results, which involves the whole limb and sometimes attains enormous proportions. This symptom is then a sign of deep-seated glandular involvement, and is a contraindication to operative interference unless for the relief of pain (Fig. 96). There is, however, always a tendency to degeneration and absorption of the cancerous growth, and so far as this goes there is a tendency consequently to spontaneous cure. The writer does not, however, find any such case reported in literature, although Billroth mentions a case of scirrhous cancer that had almost entirely disappeared, at the time of the patient's death, from metastatic deposits.

FIG. 96.—Œdema of Arm in late stages of Cancer of Breast.

Metastasis is supposed to occur through the lymphatic system in cancer, but this is probably not always the route taken by the disease. Billroth suggests that the nodules found in the lungs, the liver, and the kidneys reach those regions by embolism, a growth of cancer-cells invading the vein, being carried thence to the heart and through the pulmonary system to the varions organs. He doubts whether the disease can be transmitted by the lymphatics through the diaphragm to the liver and through the posterior mediastinum to the spinal column. In one case seen by the writer a line of infected lymphatics led along the ribs to the spinal column and thence to the liver, which was completely infiltrated with cancer. In this case there had been no return of the disease in the axilla, but one or two nodules were found in the cicatrix of the breast. The liver and lungs are most frequently the seat of metastatic deposits. The pleura may be infected by direct extension of the growth from the primary nodule through the chest-wall. These deposits may also be found in the bones and in the dura mater, and more rarely in some other internal organ. Billroth observed an appearance of the disease in the other breast several times, but the experience of most surgeons is that metastasis to the breast is an extreme rarity. It is not probable that the disease ever spreads directly from one breast to the other.

The *average duration of life* in cancer of the breast that runs its course untreated is, according to Gross, 28.06 months. In 536 cases which were operated upon, and in which the disease returned, the average duration of life was 38.5 months. The operation appears, therefore, to have had the effect of prolonging life in those cases for ten months. Dietrich's estimates place the prolongation of life at seven months. It is usually considered that after the lapse of three years from the date of operation the patient may be regarded as permanently cured if no return has been observed, the percentage of recurrence after that period being exceedingly small. Gross found that 11.83 per cent. of the cases in his collection met that requirement. A combination of the statistics of Banks, Küster, and Gross, consisting of 257 cases, shows that 19.38 per cent. were cured. The mortality of the operation amounted in this series to 12.06 per cent. In Dietrich's series of 110 cases there were 8 deaths, or a mortality of 7.6 per cent. His percentage of cures was 16.2. In a large number of cases collected from all sources Dennis estimates the cures at 25 per cent. In 71 cases operated upon by him there was 1 death from hæmophilia. His mortality was, then, 1.4 per cent., or if the hæmophilia case be excluded it was 0. Bull reports 75 cases with 3 deaths and 20 cures, the percentage of cures being 26.6, showing an increase over previous records. Richardson found that the mortality of all cases (290) operated upon at the Massachusetts General Hospital up to the year 1877 was 7.9 per cent. The mortality of the operations performed from 1877 to 1887 was 8.3 per cent., showing an increase due to the so-called "completed" operation.

The completed operation, so called, implies thorough dissection of the axilla. It has since been found necessary to dissect off the fascia of the pectoralis major muscle, and many operators have within the last year or two removed both the pectoralis major and the pectoralis minor. Notwithstanding the increasing severity of the operation, the mortality is steadily decreasing. In the writer's cases there have been but two deaths since he began to perform the completed operation. This series includes an amputation of both breasts with dissection of the axillæ, in many cases the removal of the two pectoral muscles and in one case the division of the clavicle. It would be fair to place the mortality of the writer's cases at 2 per cent.; it is probably less than that. In regard to the number of cures the writer is unable to give any figures, but he found that all those cases which passed the three-year limit proved to be scirrhous cancer. There is also one case of colloid which was operated upon in 1882, when there was no dissection of the axilla: in 1888 a nodule the size of a hen's egg was removed from the axilla that showed typical colloid cancer; since then the patient has been in excellent health.

In regard to the question of operation in the axilla, many surgeons speak of the period previous to axillary infection. Since the writer has been in the habit of dissecting the axilla in every case of operation for cancer of the breast, he has never yet found an axilla that had not already been infected, and in one case, already referred to, the operation was performed three weeks after the disease had first made its appearance as an extremely small nodule in the upper and inner quadrant.

The *diagnosis* of cancer of the breast often presents great difficulties. Although a lump in the breast of a woman between forty and fifty years of age is cancer in 80 per cent. of the cases, there is a residue in which non-malignant growths occur. The commonest form is cyst-formation due to chronic mastitis. This cyst usually develops in the upper hemisphere, and it is accompanied by the enlargement of a few glands in the axilla. These glands, however, are discrete and soft, and unlike the matted glands of cancer. The writer finds the use of the Mixter punch most valuable in such cases, and in fact in all doubtful cases of cancer. The operation when performed with cocaine injection is painless and harmless, and it secures a specimen amply sufficient for microscopic diagnosis. Chronic mastitis with fibrous thickening or tubercular abscess may be mistaken for cancer.

There remains to be considered still one form of disease which is usually described as an affection of the breast, although belonging strictly to the class of carcinoma of the skin. *Paget's disease of the nipple* has been compared to an eczematous affection limited to the nipple and the areola, which affection eventually becomes malignant and may involve the whole breast. The disease is rarely seen before the age of forty. It may make its first appearance after a confinement or after nursing, and shows itself on or about the nipple as a crust which cannot easily be removed. Presently the skin becomes red and more or less inflamed, and the nipple gradually becomes retracted. The area of the disease continues to spread, and the part becomes indurated and slightly raised above the level of the skin. The diseased surface gradually becomes more moist and bleeds easily, and finally ulceration takes place, often becoming quite deep in the vicinity of the nipple. The disease is accompanied by itching and burning. As the carcinoma grows the ulceration becomes deeper and the induration greater, and eventually it may extend into the deeper portions of the breast. Glandular involvement is rare except in the latest stages of the disease.

The histological changes observed in this disease have been studied by Paget and Porter among the earlier observers, and more recently by Thin, Darier, and Wickham. In the earlier stages the disturbance is limited, as in keratosis, chiefly to the epidermic layers. During the earliest period there are found an elevation and a thickening of the epidermis, and the cells of the rete lying between the papillæ are more abundant, and project more deeply than normal into the cutis vera. The true skin is infiltrated with small round-cells in its upper layer, but the deeper layers appear to be normal. Wickham made a special study of the psorosperms in this disease, and at this stage found them numerous in the Malpighian layer. They appear as round or oval bodies with thick glistening capsules, and they are situated in the protoplasm of the epithelial cells, pushing the nucleus to one side. When treated with alcohol the protoplasm of these bodies contracts, and leaves a space which was regarded as a vacuole in the cell. In a more advanced stage the epidermic cells are often wanting, and even the Malpighian layer is more or less destroyed, so that the papillæ are covered chiefly by round-cells. The corium is now infiltrated with an inflammatory exudation. At the beginning of the cancerous stage there is found an epithelial growth invading the corium and the various glandular structures to be found there, such as the sebaceous and sudoriparous glands and the ducts of the mammary gland. These ducts are eventually filled with pavement-epithelial cells. As these cells grow the walls of the smaller ducts give way and the epithelial growth invades the stroma of the gland. It preserves the type of epithelial cancer, and in that form involvement of the axillary glands does not take place until late in the disease. During the active stage of the epithelial growth the psorosperms have been observed by Wickham forming cyst-like structures containing a number of oval corpuscles.

The *prognosis* of the disease is favorable for cancer, for the precancerous stage may endure for many years: after the cancerous stage has developed the breast can be removed in time to forestall involvement of the axillary glands, and a permanent cure may be the result.

In the early stage the part should be treated as for eczema, but if soothing ointments fail to heal the disease, the growth can be destroyed with chloride-of-zinc paste or with solid caustic potash, or be seared with the actual cautery.

The "nitric-acid method" described by Chiene enables one to detect with greater accuracy the presence of cancer in an amputated breast. The breast should be washed in water to remove all traces of blood; it should then be submerged in a 5 per cent. aqueous solution of nitric acid (B. P.) for about ten minutes. Wash the specimen in plenty of running water, and place in methylated spirit for two or three minutes. Epithelial structures are turned an opaque white, fibrous tissue is rendered transparent, and fat is unaltered. The cut surface should be treated in the same manner. In this way the surgeon can determine more accurately than by the naked eye whether all disease has been removed.

3. Cancer of the Uterus.

The uterus, before all other organs, is the one most frequently affected with cancer. Schroeder reports that in an examination of 26,200 cases in his gynecological clinic, cancer of the uterus was observed in 812, or in 3 per cent. of all cases examined. In 7881 cases of cancer collected by Andrews, cancer of the uterus existed in 2308. Although affected so frequently with primary cancer, the uterus is more rarely the seat of metastatic cancer than any other organ. Cancer occurs in this organ in middle life or near the period of the menopause. From statistics of deaths in Vienna from 1862 to 1869 it is seen that deaths from cancer of the uterus occur most frequently from the thirty-sixth to the sixtieth year.

It may occur in early life, but it is far more rare, though usually more malignant, at that period. The figures of Williams show that heredity does not play a very important part. In 108 cases investigated, malignant disease was found to have existed in the relatives in 23 cases, or in 21.3 per cent., but in only 8 cases were the parents affected with cancer. The disease occurs most frequently in women who have borne children, particularly in those who have had large families. It is rare in the nulliparæ, and when it does occur it appears chiefly in the body of the uterus. Among the diseases of the uterus that seem to favor the development of cancer may be mentioned chronic endometritis, particularly that variety which is accompanied by glandular hypertrophy. It seems to occur more frequently in the poor than in the rich, though negresses—who are particularly liable to uterine fibroids—are far less subject to cancer than white women.

There are three principal seats of cancer of the uterus: it is found in the vaginal portion, in the cervical canal, and in the body of the uterus. Recent investigations seem to show that many of the cancers seen in the cervical canal or on the vaginal portion do not spring from the surface epithelium, but from the glandular structures in the deeper parts of the neck of the uterus, and that they appear sometimes in the cervix, and sometimes make their way out through the vaginal mucous membrane. Many of the papillary growths spring from this source (Ruge and Veit). Cancer of the neck and the cervical canal is far commoner than cancer of the body of the uterus.

The cancer of the vaginal portion develops from the epithelium of this region, and is a pavement-cell epithelioma. It is of the same type as cancer of the skin. There is an abundant stroma in which the clusters of cells are imbedded. It may grow on one or both lips. It is occasionally seen developing from the surface of an old laceration, and very rarely it occurs in the interior of the uterus. The pavement-cell epithelioma, however, does not occur so frequently as was formerly supposed to be the case, for many of the cancers of this region are of the alveolar type, resembling more the adeno-carcinomata springing from glandular structures deep in the cervix. Cancer of this part of the uterus grows frequently as a papillary tumor, and it may assume considerable size, producing the so-called "cauliflower" growth. These papillary growths may have a broad basis or they may be attached only by a pedicle. A certain portion of these cauliflower growths are composed of pavement epithelium; others, however, have cylinder epithelium, and they closely resemble the villous cancer of the bladder (Orth). Other forms of epithelioma may be flat and superficial, resembling somewhat the type known as *rodent* ulcer. The epithelial type, or cancroid, spreads outward into the vagina; it is rarely seen in the interior of the uterus or the cervix, although it may invade the cervical canal.

Carcinoma of the cervical canal is more of the glandular or alveolar type, and it is developed from the glandular structures of this region. The disease may develop here without showing itself externally before it has produced a general ulceration of the cervical canal. It may, however, grow upward and involve the cavity of the uterus, or it may grow outward into the vaginal portion. Eventually the cervix is destroyed, and when the disease is found in an advanced stage of ulceration it is difficult to decide from which region the cancer originally developed.

In cancer of the body of the uterus there is presented a type more distinctly glandular in character, the so-called "adeno-carcinoma" or malignant adenoma. Here the growth spreads deeply into the muscular tissue of the uterus, and many of the trabeculæ of the stroma contain unstriped muscular fibres (Fig. 97). The

FIG. 97.—Cancer of the Uterus (oc. 3, obj. A.).

cells in the alveoli are cylindrical, and are often arranged around a central lumen as in gland acini. Near them, however, are other alveoli, which contain solid masses of cells. These carcinomata may vary from the scirrhous to the medullary type, according to the amount of stroma they contain. By changes in the stroma there may occur a mixed form of growth, such as myxo-carcinoma or sarco-carcinoma, according as the stroma changes to mucous or to sarcomatous tissue (Orth).

As cancer of the cervix spreads the parts about become converted into one large ulcer, and the anatomical relations are lost. The cervix is destroyed, and the disease next involves the mucous membrane of the vagina, when the border of the ulcer may be raised, forming the margin of a crater. From this point the disease may spread to the subserous tissue about the uterus and at the base of the broad ligaments and the parametrium. It also extends into the wall of the uterus in a horizontal line, so that the entire thickness of the wall is simultaneously affected. Occasionally there may be found an isolated nodule of cancer higher up than the apparent upper edge of the disease. Whether this has spread by lymphatic infection, or whether it is possible that multiple cancer can form, seems to be undecided. The pathological fact, however, is extremely important in its bearing upon the choice of an operation. A curious complication sometimes occurs owing to a constriction of the cervical canal: as a result of this the secretions of the uterus are retained, and the condition known as *hydrometra* is established. In cancer of the body of the uterus the cavity may become much enlarged by ulceration before the cervical canal has been affected. This form of the disease spreads more rapidly in the direction of the peritoneum. Ulceration may, however, occur in the cervical mucous membrane from the irritation produced by the discharges. The whole organ often becomes enlarged, not simply when the body is infiltrated with cancer, but even when the disease is limited to the cervix. As the disease advances the bladder and the rectum become involved. The bladder is the organ first attacked, and a fistulous opening may eventually be established between the bladder and the vagina, and the ureters may likewise become involved in the growth. A fecal fistula is also one of the possible complications of the disease. Infiltration of the broad ligaments is often accompanied with severe pains. As the disease progresses even the bones of the pelvis may be attacked. When the disease reaches the peritoneum the intestines become glued to the fundus of the uterus, and during the process of ulceration the cavity of the uterus may open into a loop of intestine. The tubes and ovaries are affected only quite late in the disease. Lymphatic infection is found in the lumbar, retroperitoneal, and inguinal glands. Metastatic deposits in the large abdominal organs are seldom seen.

The presence of carcinoma in the uterus is not often recognized before it has reached the stage of ulceration. The earliest *symptom* is usually hemorrhage—perhaps only a slight staining, particularly after unusual exertion or after the act of coitus. It may, however, appear in the form of profuse menstruation, or it may come on after the menopause as a frequently-recurring hemorrhage. Of sixty cases examined by Gusserow, in no less than fifty was hemorrhage the first symptom.

When the ulceration becomes more extensive there is often a watery discharge, which later may become sero-sanguinolent. In the papillary form of cancer the discharge may be purulent and be mixed with foul fragments of sloughing tissue. Pain is often entirely absent. The attacks of internal pain sometimes accompanying the disease indicate an extension to other organs or in the direction of the peritoneum. Irritability of the bladder or of the rectum is caused by the gradual involvement of these organs in the cancerous infiltration. More rarely there may be pruritus or pain in the breast or symptoms of nausea. In advanced stages of the disease there may be symptoms of localized peritonitis.

A singular lack of constitutional disturbance often continues for a long time, but later the foul discharges may occasion sepsis which, combined with uræmia, may produce typhoidal symptoms. With the development of the cancerous cachexia comes emaciation, and the patient eventually succumbs with the symptoms of marasmus. The duration of the disease may vary greatly. Its course is usually more rapid than that of cancer of the breast, and the patient succumbs in most cases in from six to twelve months from the appearance of the first symptoms.

Many attempts have been made to determine the nature of the malady from the local appearances, but the only certain way of settling definitely the question of *diagnosis* is by microscopic examination. For this purpose fragments scraped away are almost useless; pieces of considerable size should only be used for this purpose. Frequently, however, it is possible only to obtain scrapings, particularly in cases of malignant adenoma. In this case the scrapings should be rolled up while fresh into a ball and hardened in alcohol. Sections can then be taken from this mass for examination. If there are found in these scrapings typical glandular structures, perhaps with ciliated epithelium within the tunica propria, and a round- or spindle-cell stroma, the surgeon has to do probably with hyperplasia of the mucous membrane. If, however, there are found irregular alveoli filled with epithelial cells or an anastomosing network of epithelium containing possibly epithelial balls and a stroma in which muscular tissue is found, the diagnosis of carcinoma may be made. The presence, on the one hand, of tubular masses of gland-like tissue, very closely packed together without any tunica propria or muscular tissue, is strongly suggestive of malignant disease. On the other hand, an irregular glandular growth, consisting of dilated acini or of acini filled with cells or papillary growth situated in a normal stroma, is not sufficiently typical of cancer to establish a diagnosis (Orth).

The old *operation for cancer of the uterus*, consisting in local excision or cautery, was almost invariably followed by a prompt return of the disease. The modern operations show better results. High amputation of the cervix is not a dangerous operation, and it shows good results, but it is less frequently employed now that more radical methods have come into use. Baker reports sixteen cases of high amputation with no deaths. In six the disease recurred, and in ten there was no recurrence at periods varying from two to eight years. Hofmeier performed thirty-three high amputations with only one death. The after-results are reported by him to be as good as those for total extirpation.

The early statistics of abdominal and vaginal hysterectomy show a large mortality. Thus in 1885 Duncan reported 137 cases of abdominal hysterectomy, with 99 deaths, or a mortality of 72 per cent. In 276 cases of vaginal hysterectomy there were 79 deaths, or a mortality of 28 per cent. Sarah E. Post, in 1887, collected 722 American cases of vaginal hysterectomy, with a mortality of 24 per cent. Scheyron, in 1890, reported 337 vaginal hysterectomies, with a mortality of only 16.9 per cent. Of 854 cases of vaginal hysterectomy collected by Richardson and Stone for the writer—which cases were operated upon between 1887 and 1892—there was a mortality of 9.48 per cent. In 483 cases of vaginal hysterectomy collected from reports in which an attempt had been made to furnish results, it was found that in 53 there was no recurrence at the end of two years; in 26, no recurrence at the end of three years; in 14, no recurrence is reported at the end of four years; and in 38, no recurrence was reported at the end of five years. In 34 cases the disease recurred at the end of the first year; in 45, recurrence was reported at the end of the second year; and in 2 only was the disease known to have returned during the third year.

4. Cancer of the Tongue.

Cancer of the tongue is invariably of the pavement-epithelium type, or epithelioma, such as has already been described in Cancer of the Skin. The cancer springs from the epithelial layer of the mucous membrane, but never from the glandular apparatus of the tongue.

The disease is much commoner in men than in women. In 122 cases reported by Billroth there were 6 in which the disease was observed in women. In 293 cases reported by Barker there were 46 females. In a collection of 991 cases 151 were women. Statistics show that the percentage of women as compared with men varies from 43 to 33 per cent. The writer remembers having seen the disease certainly four times in women, one of whom, at least, was addicted to the use of a pipe. It occurs most frequently between the ages of forty and sixty-five, although it is occasionally seen at a much earlier period, as the writer has operated at least once upon a man not yet thirty years of age.

Cancer is found in all parts of the tongue, but more frequently in the anterior half than in the posterior half, and on the edges rather than on the median line or dorsum, though it is seen occasionally on the posterior portion of the tongue near the papillæ circumvallatæ and in the region of the frenum.

Occasionally two carcinomata may be found upon the same tongue, both of them being primary growths. The writer has observed this condition in one case, both nodules developing almost simultaneously and at some distance from each other. There may also be seen secondary nodules or a diffused form of cancer in the tongue; which fact is of importance to remember in making the selection of an operation.

In no region of the body does the origin of the disease appear more clearly due to previously existing irritation. The presence of carious teeth, the foul condition of the mouth, the eating of highly-spiced food, the use of alcoholic drinks, and the "rough eating" indulged in by men may account partly for the greater frequency of the disease in the male sex. All authorities agree that a very large proportion of the cases of cancer are preceded by various abnormal conditions of the surface of the tongue. These conditions are variously described as chronic glossitis, psoriasis, icthyosis, smoker's patch, leucoma, or leucokeratosis. The latter condition strongly resembles that which has already been studied in the morbid conditions of the skin preceding cancer. Leucoma may assume various forms, but the commonest form is a patch or patches of white furry membrane, which patches appear to be somewhat thicker than, and therefore slightly raised above, the surface of the surrounding membrane. The patches seen by the writer were very white and in striking contrast to the red mucous membrane. They were limited to the side of the tongue, and they covered the border rather than the dorsal surface. The whole surface of the tongue may be affected in this way. Associated with this condition are numerous fissures and small ulcers which appear from time to time. Warts are also liable to form in the latter stage of the disease, and, according to Butlin, a wart on a leucomatous base never gets well and always becomes cancerous. These conditions have been called the "pre-cancerous stage," and the frequency with which cancer seems to follow such conditions both on the skin and in the mucous membrane appears to justify the expression.

According to Wallenberg, leucoma—or "leucoplakia," as it is often called—is caused most frequently by the irritation produced by the volatile and empyreumatic oils of tobacco. It may also be caused by disturbances in the digestive tract, with which of course the tongue sympathizes. Syphilis is also supposed to be a predisposing cause. A section made through a leucomatous patch shows a growth of the epithelium of the rete mucosum both upward and downward. According to Butlin, the papillæ are obliterated, but in a section made by Gannet, a drawing of which is before the writer, the interpapillary epithelium seems to be elongated downward. There is a thickening also of the epidermic layer. The papillary layer is infiltrated with round-cells. Such a condition strongly resembles that seen in keratosis senilis, and it could with propriety be called "keratosis linguæ." Leucoma is almost unknown in persons under twenty years of age. It appears rarely to begin in persons over sixty, and it seldom attacks women (Butlin).

The writer has seen but few cases of leucoma—one in a lady on whose tongue it first appeared in youth, and remained in the shape of several large brilliant white patches until old age, when it disappeared; in another case, a man forty-three years of age, the tongue had been troublesome from childhood; the mucous membrane was sensitive and easily irritated, and it was prone to inflammatory conditions, during which small ulcers appeared. At the age of thirty-four typical leucoma appeared, situated for the most part on the right side of the tongue. Three years later the patches enlarged and a warty growth formed in the centre. Three years after this the writer removed with the knife the largest patch, which was about the size of a silver half-dollar. This operation was performed in June, 1891. In October, 1891, a small epithelial growth of an apparently malignant nature appeared on the *opposite* side of the tongue. This growth was removed, and it was found to be typical cancer. In December a similar growth was removed from the tip of the tongue. In April, 1892, both growths having reappeared, a large portion of the left side and the tip of the tongue was removed by a wedge-shaped incision. The disease never returned in the tongue, but six months afterward a glandular enlargement was observed under the left jaw, and the patient died two months later. The growth was found to be typical carcinoma.

In the case above alluded to the writer had an opportunity of observing the earliest stages of the cancerous growth, as it was shown to him but a few weeks after it had made its appearance. It even then had an unmistakably cancerous aspect. There was a distinct infiltration of the tissues of the tongue, and the growth was surrounded by the pearly rim so characteristic of epithelial disease.

When fully developed the cancerous growth usually breaks down in the centre and presents itself as an ulcer with indurated and elevated margins. Such ulceration occurs in cancers situated on the side of the tongue and subjected to friction against the edges of the teeth. It may appear also on the side of the tongue as a nodulated mass in the form of a rosette, without any tendency to ulceration. As the disease grows the fold of mucous membrane extending to the jaw becomes involved, and the tongue is bound down by the contractions that occur to the floor of the mouth. When these ulcers are situated near the base of the tongue, the anterior pillar of the palate, and eventually the tonsil and the wall of the pharynx, become involved.

Less frequently the disease begins as a nodule in the substance of the tongue, which nodule slowly enlarges, and finally shows itself above the surface. More rarely still the disease appears to originate beneath the floor of the mouth, and never comes to the surface, but it is felt as a hard, indurated mass beneath the chin. The tongue is so drawn down as to be deeply indented at some one point, and speech, and even swallowing, are often materially affected. In one such case that the writer has under observation the patient is greatly distressed by a constant flow of saliva. The enlargement of the lymphatic glands occurs at varying periods during the progress of the disease. Usually the glands do not appear to be affected until several months after the first appearance of the disease in the tongue.

Many cases are on record where the tongue has been removed, in which event there has been no subsequent manifestation of the disease. It is, however, not an uncommon occurrence to find a return of the disease, if such an expression may be used, in the lymphatic glands, while the tongue remains healthy. In such a case it is clear that the gland in question was already affected at the time of the operation, but that it was too small to be felt. Kocher mentions a case in which glandular infection occurred in five weeks, and the writer has seen one where the glands were infected equally early in the disease. The writer is so strongly impressed with the danger of leaving such an infected gland that he should not be contented to operate upon a case of cancer of the tongue without exploring the glandular region. He has, however, followed one case for two years in which half of the tongue was excised through the mouth and no glands were sought for. There was at the last report no evidence of disease, but such a result is hardly sufficient to authorize a repetition of the operation in the light of the usual experience.

The most frequent *seat of glandular infection* is the floor of the mouth and the submaxillary region. A gland may be felt in front of the sterno-mastoid muscle and at the side of the thyroid cartilage. The glands of the neck are quite as likely to be involved as are the glands of the axilla in cancer of the breast, and the writer has no doubt that the small percentage of cures reported is due to the fact that "completed operations" are not so frequently performed as they should be. Occasionally there is seen an extensive enlargement of the submaxillary and cervical glands, with little or no primary disease of the tongue. In a case which came under the writer's observation the upper triangle of the neck was so filled with enlarged glands as to form a tumor of considerable size. The tongue presented the appearance of the so-called "fern-leaf" pattern, but there was only slight induration, and it was difficult to say exactly where the primary lesion was situated.

As the disease progresses in the mouth the ulceration increases, and the interior of the mouth becomes converted into a foul crater. The pain, which at first is usually slight, becomes severe, and it radiates in the direction of the ear, and a great deal of acute pain is often experienced in the later stages of the disease. The glands of the neck become enormously enlarged, and they form a tumor filling out the side of the neck from the jaw to the clavicle. The trachea is often pressed over under the opposite ear, and the rings can be felt beneath the skin; but difficulty of breathing is rarely experienced, although it may be impossible for the patient to swallow solid food. Metastatic deposits are said to be comparatively rare, but they may be seen in the lungs, the liver, and the kidneys. Death may occur from hemorrhage or from exhaustion.

The diseases most likely to be mistaken for cancer are simple ulcers formed by the friction of the sharp edge of a displaced tooth, syphilis, and tubercle. In the case of the simple ulcer the position of the lesion, when the tongue is in its natural position, usually indicates sufficiently clearly the origin of the affection. The removal of the tooth is promptly followed by healing of the ulcer. In syphilis there is usually an induration of the substance of the tongue rather than a new growth of tissue: the disease is said to be found more frequently upon the median line than cancer. Tuberculosis of the tongue occurs as a chronic inflammatory process, and it appears as an ulcer with a more or less ill-defined inflammatory infiltration of the adjacent parts, whereas cancer does not produce an inflammation of the surrounding tissues. The line between the healthy structures and the new growth is therefore usually well marked.

In all uncertain cases—and they are numerous—a fragment should be removed for microscopical examination, and this removal can be effected in no better way than by the Mixter punch.

Cancer of the tongue runs a comparatively acute course, the duration of life varying from six to eighteen months from the first appearance of the disease.

The operations for removing the tongue vary greatly, and they may in general be classified under three heads. Formerly a large number of cases were operated upon by the *écraseur*, owing to the fear of hemorrhage, and many operators still prefer this method, but it is rapidly going out of use. Whitehead's method of removing the tongue through the mouth with scissors has replaced the older operation. It consists in a rapid excision of one-half or the whole of the tongue with the scissors, care being taken to keep the mouth well open during the operation. Hemorrhage is prevented by the use of hæmostatic forceps, which seize the lingual arteries either before or as they are divided. In the third group belong those operations which contemplate an incision for the purpose of exposing the submaxillary and cervical glands, and the removal of the tongue either through the mouth or through the incision thus made. The submental incision, which enables the operator to remove the tongue through the floor of the mouth, is a useful method in case of cancer near the frenum or in the apex of the tongue. The submaxillary incision exposes the upper triangle of the neck, and enables the operator to remove the infected glands in this region before the mouth is opened, and the tongue is drawn through the wound. This method is sometimes called "Kocher's operation," and it is frequently preceded by tracheotomy in order that the wound in the mouth may be treated antiseptically.

The operation preferred by the writer consists in an incision directly downward from the corner of the mouth to the lower edge of the jaw, and thence backward to the angle of the jaw. After the cheek is reflected the jaw is divided at a point opposite the disease. A vertical incision downward from the wound exposes the infected gland region of the neck. Through a wound thus made the whole infected area may be removed in one continuous mass.

The mortality of operations upon the tongue for cancer is somewhat difficult to obtain, owing to the great variety of operations and to the varying degrees of severity of the disease. The causes of death are usually bronchitis, pneumonia, or gangrene of the lung. The German expression *schluck-pneumonie* suggests the infective nature of the process. Death rarely occurs from hemorrhage or from shock. In 139 cases reported by Whitehead there were 20 deaths, showing a mortality of 14.3 per cent. Separating the cases where the tongue alone was removed from those in which the glands and the jaw were involved, it is found that in the former cases the mortality was only 4.5 per cent., whereas in the more complicated operations where the glands were involved the mortality ran as high as 77 per cent., and where a portion of the jaw was also involved as high as 57 per cent.

In a series of 58 cases reported by Kocher, belonging to the class of "glandular" or "completed" operations, in which the most strict antiseptic precautions were observed, the mortality was only 10.3 per cent. These results are better even than those following the use of the écraseur. A series of 40 cases reported by Barker operated upon in this way gives a mortality of 12.5 per cent. Billroth's clinic gives a mortality of 10.1 per cent. in 148 cases. This mortality is a marked diminution from that in his earlier cases, which at one time was as high as 25 per cent.

The results of treatment in this disease cannot be said to be encouraging. In the series of 148 cases just alluded to there were only 10 cases that remained well at periods varying from fourteen months to eight years. On an average the patients died one year after the operation from a return of the disease. In 38 cases in which reports were obtained by Kocher it was found that the disease had returned in 25. The earliest return appeared within seven months, and in one case the disease did not appear until ten years after the operation. In the 13 cases in which there was no return reported, 5 were found well at the end of seven, eight, ten, and twelve years, respectively. In Barker's series of 170 cases there were less than five who were well three years after the operation; and in Butlin's 70 cases there were but 6 cases of cure on the three-years' limit. Richardson obtained 13 answers from 20 cases operated upon at the Massachusetts General Hospital. Of these cases 11 were dead, and of the 2 living cases it is uncertain whether one of them was cancer.

It will be seen that the best results thus far reported have been obtained after Kocher's operation. The very small percentage of permanent cures reported by nearly all surgeons may in part be accounted for by the imperfect nature of the method of operating employed. Few surgeons are content at the present time to remove the breast without a dissection of the axilla, but the number of those who attempt a dissection of the strategic points in the neck in cancer of the tongue is yet small. In the writer's opinion the whole neighborhood of the infected region should carefully be explored for disease, and in a majority of cases it is advisable to perform temporary section of the jaw in order to expose thoroughly the seat of the trouble. It is only by such radical measures that it can be hoped to reduce the fearful mortality of cancer of the tongue.

5. Cancer of the Œsophagus.

Carcinoma is one of the most frequent forms of disease of the œsophagus. It belongs to the pavement-epithelium type of carcinoma, and on microscopic examination epidermic balls are found here and there among the clusters of epithelial cells. It develops from the epithelium of the mucous membrane or from the ducts of the mucous glands. Colloid cancer of the œsophagus is said to be extremely rare. Butlin refers to a scirrhous type in which the progress of the disease is unusually slow. The disease is said to occur oftener in men than in women, although the writer has seen it in about an equal number of each sex. Of 510 cases analyzed by Newman, 108 were women and 402 were men. It is most frequently found in persons over forty years of age. Mackenzie in a study of 100 cases found 92 in which the patients were over the age of forty. The seat of the disease varies greatly. Rindfleisch places it in the middle third of the œsophagus, particularly at the point where the left bronchus crosses the œsophagus. Mackenzie found the disease in more than half the cases in the upper half of the œsophagus. Petri and Zenker, however, found 63.8 per cent. of the cases in the lower third. Newman states that the commonest spot in his experience is behind the cricoid cartilage. The writer found it usually below the level of the cricoid cartilage or on a level with the upper edge of the sternum: in one case he saw it at the junction of the pharynx and œsophagus. The disease usually encircles the tube and causes a firm constriction. When the œsophagus is laid open the disease appears as an ulcer with elevated and everted edges. The width of the carcinomatous ring varies from 2 to 8 cm., but it may rarely be much more extensive.

As the disease progresses the ulceration becomes more extensive, and perforation may take place into the trachea or the bronchi, the posterior mediastinum, the pleura, the pericardium, or the blood-vessels. Perforation of the trachea is a not infrequent complication, and it can be recognized by the presence of a muco-purulent expectoration containing particles of food. The growth may press upon the recurrent laryngeal and pneumogastric nerves. Metastatic deposits are found in the adjacent lymphatic glands, and not infrequently in the lungs, the liver, and the kidneys.

The *first symptom* of the disease is, in the majority of cases, difficulty in swallowing. On questioning the patient a history of loss of flesh during the previous six months may usually be obtained. As the disease progresses a tumor can be felt in the region of the neck or the cervical glands are perceptibly enlarged. The presence of a cough shows that the disease has begun to infringe upon or to involve the tracheal wall. The passage of a bougie will usually settle the diagnosis, for strictures from any other source except from swallowing corrosive liquids are extremely rare.

The *treatment of cancerous strictures* formerly consisted in the frequent passage of bougies, but this method is liable to be followed by perforation of the softened tissue. Symonds devised a method of œsophageal tubage which is far superior. Symonds' tubes are about 4 inches in length, and have a funnel-shaped opening which permits them to be introduced and left in the stricture; a ligature attached to the end of the tube emerges from the mouth and is fastened to the ear. Mixter devised an ingenious method of sounding the narrow strictures and of dilating them, and he has improved Symonds' method of introducing the tubes. These tubes can be worn for several days at a time with great comfort. This method supersedes largely the formation of a gastric fistula.

Gastrostomy, as originally performed, established a fistula through which the patient could easily be fed. The operation provided no means of preventing the escape of the contents of the stomach through the fistulous opening. The cough with which patients in the advanced stage of cancer of the œsophagus are afflicted often favors leakage through the fistula. Several operations have been devised to overcome this difficulty. Von Hacker makes the fistula through the left rectus muscle, so as to secure a sphincteric action from the tonic contraction of its fibres around the extruded portion of the stomach-wall. Witzel aims to combine a sphincter-like action of the muscles of the abdominal wall with a valvular fistula. The fistula passes through both the rectus and the transversalis muscles, whose fibres, running at right angles to each other, may be expected to contract still more efficiently than the rectus muscle alone. The second feature of this operation is the unfolding of a tube in the wall of the stomach, which is stitched over the tube so as to form an oblique canal. This method is said efficiently to overcome the tendency to leakage from the stomach. A third method, described by Meyer as the Ssabanejew-Frank method, consists in drawing out a loop or cone on the stomach-wall through the ordinary oblique incision, and passing it under a bridge of skin to a point above the border of the ribs, where it is fastened and opened. This operation has not as yet had an extensive trial, but Meyer, in a review of these various methods, looks upon it as the coming operation in cases of malignant œsophageal stenosis. The writer has succeeded in establishing a gastric fistula with perfect valvular action on a dog by the following operation: A fold of the anterior wall of the stomach is pinched up and stitched one and a half inches higher up on the surface of the organ. If an incision is made into the stomach just below the line of suture, a double fold of mucous membrane will be found hanging over the inner opening of the cut. In the stomach of Alexis St. Martin a similar fold of mucous membrane covered the internal orifice of the fistula. According to Knie, the average duration of life in thirty-five cases successfully operated upon was one hundred and twenty-five days. Tracheotomy may be necessary on account of œdema of the larynx or pressure upon the recurrent laryngeal nerve. Œsophagectomy was performed in 1877 by Czerny for a small growth in the œsophagus, the lower segment of which was united to the external wound. Ashurst collected twelve cases of œsophagectomy with eight deaths. If the growth could be discovered early enough, such an operation might be contemplated with a view to a radical cure of the disease.

6. Cancer of the Larynx.

Cancer of the larynx appears usually as a pavement-cell carcinoma; rarely an encephaloid or a scirrhous form exists in the larynx. Cancers of this region are divided into *intrinsic* and *extrinsic*. Intrinsic cancer includes growths originating from the vocal cords, the ventricular bands, and the ventricles. Extrinsic cancer is situated upon the epiglottis, the ary-epiglottic folds, and the interarytenoid region.

Cancer of the larynx is a disease of advanced life, 50 per cent. of the cases occurring between the ages of fifty and seventy. Males are more liable to the disease than females. The abuse of tobacco and strong alcoholic drink, prolonged residence in humid, cold climates, as well as respiration of gases or of vapors of an irritating nature, are predisposing causes (Morgan).

Intrinsic cancer has at first the appearance of a wart-like growth taking its origin somewhere in the middle or the upper portion of the larynx, from the vocal cords, or the margin of the ventricle. Ulceration takes place at an early period, and it infiltrates the surrounding parts, involving the cartilages and eventually spreading beyond the limits of the organ. The lymphatics are infected ultimately, but only to a limited extent Metastatic deposits are probably exceedingly rare, as death occurs in the majority of cases from changes produced by the local conditions.

Extrinsic cancer originates in the epiglottis or the ary-epiglottic folds or anywhere on the upper margin of the larynx. From this point it spreads to the surrounding parts, and it may involve the pharynx, the tongue, the tonsils, and the palate. The lymphatic glands are infected early in the disease.

The earliest symptom of this disease is hoarseness; later there may be difficulty of breathing and of swallowing. Pain, which at first is dull, may later be of a sharp, cutting character, and it extends to the ear, cheek, and neck of the affected side. There is cough, with a more or less foul, purulent expectoration.

An early diagnosis of the disease is of the greatest importance, for there may be sarcoma as well as cancer in the larynx, in addition to the many benign forms of growth, and tubercular and syphilitic ulceration may exist within the larynx. The removal of a fragment for microscopical examination should, according to Newman, not be done until it is decided to operate immediately if the growth prove to be carcinoma, as the growth often becomes more malignant after such an operation.

The *prognosis* is unfavorable in all forms of cancer of the larynx, but it is much worse in extrinsic cancer. In intrinsic cancer the disease progresses slowly and death may not occur for several years.

Patients affected with extrinsic cancer die usually at the end of a year or eighteen months. The *treatment* may be palliative or be operative. Under the former heading comes tracheotomy, which often relieves many of the most distressing symptoms of this disease. The principal operations are thyrotomy and unilateral or complete laryngectomy. The mortality of total extirpation of the larynx has decreased somewhat within the last ten years, but it is still quite high.

In 121 cases compiled by Newman there were 41 deaths, or a mortality of 33.88 per cent. In 55 partial extirpations there were 16 deaths, or a mortality of 29.09 per cent. The results of operation in cases of intrinsic cancer show that after total extirpation of the larynx 16 per cent. of the cases remained well at the end of three years, and in partial extirpation the percentage of cases of intrinsic cancer remaining well after three years was 17.40. The number of operations is now exceedingly large, and many have been performed in America. In carefully-selected cases, such as that recently reported by Monks, where the disease was confined to the vocal cord and the patient remained well in active work eighteen months after the operation, it is reasonable to hope that a permanent cure may be effected.

7. Cancer of the Stomach.

Cancer of the stomach is one of the commonest forms of carcinoma. It takes its origin from the cells of the gastric follicle, and as the disease develops it perforates the muscular layer and then spreads rapidly. The commonest variety is the cylinder-cell cancer, which may appear both as a medullary and as a scirrhous form, and colloid cancer is also occasionally seen. The disease attacks men slightly oftener than women. It is rarely seen before the age of thirty, three-fourths of all cases occurring between the ages of forty and seventy. The most frequent seat of the disease is at the pyloric orifice. Welch analyzed the reports of 1300 cases, and found the pyloric region the seat of the disease in 60.8 per cent. The growth shows a tendency to break down and ulcerate. At times this tendency is so great that only a small margin of cancer remains, as in rodent ulcer of the skin. At other times the growth is very exuberant. Metastatic deposits in the lymphatic glands and the abdominal organs are frequent accompaniments of the disease.

The principal symptoms are pain in the epigastrium, with symptoms of dyspepsia, vomiting, the development of a perceptible tumor, and emaciation.

The disease may be regarded as incurable, but attempts have been made during the last decade to remove the growth by resection of the pylorus. Billroth, the originator of this operation, reports 29 operations with 16 deaths. Of the 13 who survived the operation, 5 died within ten months after the operation; 2 lived over one year; 1 lived one and a half years; 1 lived two and a half years; and 1 lived five and a quarter years. Only 2 patients remained well at the time of the report, but in 1 the operation had been performed only four and a half months before, and in the other two and a half months before. The total number of cases reported at the Berlin Congress was 56, with a mortality of 48.2 per cent. Among the most recent reports are those of Czerny, who gives 12 operations with 5 deaths: 2 were living in complete health fifteen and twenty-six months after the operation. The other 5 died two, seven, ten, fifteen, and eighteen months, respectively, after the operation, with symptoms of a return of the disease.

8. Carcinoma of the Intestines.

Carcinoma of the Intestines.—The most frequent seats of carcinoma of the intestines are at the ileo-cæcal valve, the descending colon, and the sigmoid flexure. Cancer may, however, occasionally be seen in the small intestine. Of 37 cases collected by Butlin, 32 were in the large intestine and 3 in the small intestine, the seat of 2 being uncertain. In 4 cases the disease was in the ascending colon; in 3, in the transverse colon; in 7, in the descending colon; and in 9, in the sigmoid flexure. The variety usually seen is the cylinder-cell carcinoma, which may at times assume the medullary or the scirrhous type. Colloid cancer is also found in this locality. Ulceration begins early, and cicatricial contraction accompanies it, so that the disease may appear as a narrow fibrous stricture with little if any new formation. At other times considerable length of the bowel may be affected. As the disease progresses the muscular coat is perforated and the peritoneal coat becomes infiltrated. As a result of this infection, adhesions occur to adjacent peritoneal surfaces, and the diseased gut becomes so bound down that an operation for resection or one for intestinal anastomosis is rendered exceedingly difficult: sometimes it is impossible to perform either operation. Death occurs usually as the result of chronic obstruction of the bowels. According to Butlin, the duration of the disease is short. From the beginning of the symptoms to the time of death the period varies from six to eighteen months. The disease attacks males and females about equally. It occurs generally after the age of forty years.

Operative statistics collected by Weir and Butlin show a high mortality. In 37 patients reported by Butlin on whom the operation was performed, 18 died shortly afterward. In only one instance among those who survived the operation was there a patient still well at the end of a year. Czerny reports 10 cases of resection for malignant growths—4 at the cæcum, 2 at the sigmoid flexure, 3 in the transverse colon, and 1 in the descending colon. In 3 cases an adjacent coil of intestine was involved; 1 was a medullary cancer, 1 was a papillary growth, and 4 were adeno-carcinomata; of the latter four, 3 were of the scirrhous type; 3 were cases of colloid cancer, and 1 case proved to be an alveolar sarcoma which appeared five years after the removal of an ovarian sarcoma. This patient remained well six years after the resection of the intestine. Of the cases, 5 recovered from the operation and 5 died. Of the five recoveries, 1 died six months afterward from local recurrence, and 4 were alive six, fifteen, nineteen months, and six years respectively after the operation. Of the patients, 6 were women and 4 were men. The men all died from the effects of the operation. The average age was forty-five years. Czerny regards the most favorable cases for operation those of the scirrhous type, which cause stricture early and thus lead to operation.

9. Cancer of the Rectum.

Carcinoma when found at the anus is of the pavement-cell variety, and when growing from the mucous membrane it appears as a cylinder-cell carcinoma. There are, therefore, in this locality both types of the so-called "epithelioma." The pavement-cell form, which takes its origin in the cutaneous coverings of the anus, begins as a warty or papillary growth that breaks down early and ulcerates. It is not unlike cancer of the lip in its early stages. The surrounding parts are more or less hard and infiltrated, and the edges of the ulcer are elevated and sharply defined. The growth spreads inward and involves the mucous membrane, and it invades also the external integument, involving the perineum or the commissure of the vagina and the labia in women.

The cylinder-cell carcinoma (Fig. 98), which develops from the follicles of Lieberkühn, begins as a more or less exuberant growth, which soon breaks down and develops into a crateriform ulcer involving more or less of the circumference of the bowel. This growth is found some little distance within the rectum, and it is often difficult for the exploring finger to reach its upper margin.

FIG. 98.—Cancer of the Rectum (oc. 3. obj. A.).

The cells are arranged in acini, and they have a strikingly glandular appearance, closely resembling that seen in cancer of the uterus (Fig. 99). It is therefore often called "adeno-carcinoma" or malignant adenoma. This is the commonest variety of cancer of the rectum.

FIG. 99.—Cancer of the Rectum, showing cylinder-cells (oc. 3 obj. D.).

Cancer occurs also in the medullary form, but more rarely. It is exceedingly malignant, and it soon infiltrates the walls of the rectum, converting the latter into a rigid tube and gluing it to surrounding parts. Scirrhous cancer is said to occur high up near the sigmoid flexure or in the neighborhood of the prostate. It infiltrates the submucous tissues, and the mucous membrane over it for a time appears healthy. It grows slowly and causes annular stricture, or it is felt as a hard nodule in the wall of the rectum. Colloid cancer appears as a diffuse infiltration of the mucous membrane that spreads to the deeper parts. It is, however, a rare form of cancer in this region. Villous cancer is occasionally also seen.

Cancer of the rectum occurs usually in middle life or in old age. There are, however, exceptions to this rule, cases having been rêported in youth and even in childhood. In a collection of 107 cases, Kelsey found 50 cases in males and 57 in females.

As ordinarily seen, cancer of the rectum forms a large crateriform ulcer, with raised edges, encircling the bowel, and it is situated two to three inches from the margin of the anus. As it grows it spreads chiefly to the deeper parts. As the surrounding layers become involved there is great destruction of tissue; contraction consequently takes place, and a long, narrow stricture forms, the walls of which are made up of the cancerous growth. In the female the vagina and the uterus become attached to the growth, and in the male the prostate and the bladder are invaded. The growth may extend also to the sacrum. As the walls of the adjacent organs give way before the advance of the disease, fistulæ are established and fæces may be discharged in the urine or urine may flow into the rectum.

Cancer of the rectum remains for some time a localized disease. In 47 autopsies reported by Iversen there were no metastases in 21. After a certain period of time the lymphatic glands in the perirectal fat become enlarged, and the infection spreads along the pelvis into the abdominal glands. When the disease is situated near the anus the glands of the groin may become involved, and, according to Czerny, this form of cancer is much more likely to recur after operation.

The duration of the disease is seldom more than two years, although instances have been recorded in which the symptoms have existed for as many as five or six years. Patients sometimes die, however, within a few weeks or months of the first appearance of the symptoms of rectal affection (Butlin).

The early *symptoms* of the disease are often mistaken for hemorrhoids. The breaking down of the new growth gives rise to a bloody or muco-purulent discharge which is mistaken for diarrhœa. Later, the constriction causes apparent constipation, with intercurrent loose discharges or tape-like stools. Accompanying this condition there may be a certain amount of ill-defined, colicky pain. As the growth increases there is a sense of weight or deep-seated pain in the pelvis or the back. In the more rapid-growing forms of cancer the pain may become excruciating as the new growth forces its way into the tissues. Later the symptoms of obstruction are observed. Cachexia in the later stages of the disease is very marked. Cachexia is caused partly by the disease and partly by the septic absorption from the bowel and the secondary affection of other organs.

The operation that was formerly employed for a radical cure of the disease was known as the "Lisfranc" operation, and it consisted in an excision of the bowel from below. Statistics compiled up to 1881 show a high mortality, varying from 31 to 58 per cent. in the hands of different surgeons. During the next ten years the improved methods produced a considerable reduction in the death-rate. Thorndike estimates the mortality of the operations of various kinds done during this period in a selected series as low as 16.1 per cent. Butlin collected 100 cases, including part of both periods, with a mortality of 35 per cent. Of the 65 patients who survived the operation, all were not subsequently heard from, but 13 cases were reported alive and well for at least two years after the operation. Iversen in an analysis of 247 cases of all kinds of operations found in 70 patients who survived the operation (but who died subsequently) that there was a local recurrence in 42, and in 32 cases that were still living there were 6 with local recurrence of the disease.

Kraske's method was first described in 1885: it consists in a posterior incision with resection of the coccyx and a portion of the sacrum. There are other operations of a similar nature, but differing in the amount of bone resected. This operation, although it is more severe than the earlier method, does not appear to be much more dangerous. A collection of 102 cases operated upon in this way gives a mortality of 21.5 per cent., though Thorndike's collection of cases gives a mortality of only 14.7 per cent.

It is early yet to determine the merits of the modern operation as a curative measure. Arnd, in a collection of 98 cases operated upon by various methods, reported 24 "cures" (time-limit not stated), and of these he found 15 had been operated upon by the modern method. Of 39 cases operated upon by Albert, 3 were well one year after operation, 2 were well two years after operation, 1 had passed the three-year limit, and 1 was well four years after operation.

The number of cures by any method is not yet known to be large. The disease is, however, in many cases exceedingly slow in its course, and if cases are carefully selected for operation it seems probable that the future will show an increased percentage of cures.

10. Carcinoma of the Bladder.

Cancer may grow from the walls of the bladder or from the prostate gland. Cancers growing from the latter organ are in no way to be distinguished clinically from those of other regions of the bladder, and they form a large proportion of the malignant growths in the vesical cavity.

The precise origin of carcinoma at the neck of the bladder is indeed difficult to determine, and even those carcinomata situated more posteriorly at the base of the bladder are uncertain in their origin, as the middle lobe of the prostate may have prolongations extending some distance into the walls of the bladder, and the disease may be found to spring from these glandular bodies, as in a case reported by Marchand. The epithelium of the acini of the prostate is a short cylinder-epithelium, and in the deeper more spongy portions of the prostate it is cubical. A small-cell carcinoma with a glandular arrangement of the cells in the alveoli is strongly suggestive of prostatic origin. There are, however, forms of carcinoma that spring from the bladder-wall directly, although Klebs claims that such do not exist. Bode found that in 30 cases of cancer of the bladder 14 were in women.

Orth describes the villous cancer as the commonest form. There may be a benign papilloma appearing as a villous tumor, and also a villous cancer. In the papilloma are found very long fimbriated processes composed of a connective tissue in which run blood-vessels covered by several layers of columnar cells. In the villous cancer are found similar villi, and in the base of the tumor at the point of origin of the broad villi and also in the bladder-wall are found alveoli containing cancer-cells. The villi are, however, as Küster shows, merely an accidental feature of these growths, and indicate nothing as to the microscopical character of the tumor.

Cancers of the bladder-wall spring from the deeper layers of the epithelium and rarely from the epithelium of the mucous glands.

The commonest form of cancer of the bladder, according to Küster, is that composed of squamous and pear-shaped cells, a polymorphous type with cells resembling those of the bladder-wall. There is an abundant connective-tissue stroma which produces a scirrhous type of cancer. The medullary form is much less frequent. Sometimes the cells assume the pavement-epithelium form, producing pavement-cell carcinoma or epithelioma, such as is seen in the skin. In these cases well-marked epithelial nests or epidermic balls may be found. Colloid cancer may also occur here. This condition may involve the whole or only a part of the growth. All these varieties appear as rounded, more or less flattened elevations in the mucous membrane. The membrane may run smoothly over the growth, or it may be infiltrated, or, finally, papillary growths may develop on the surface of the tumor. A papilloma may precede the development of a cancer for several years, and Küster suggests that the irritation produced by the pull of the tumor upon the mucous membrane during urination may be a source of irritation which gives rise to the cancerous growth. The conditions resemble those in the skin where warty growths precede epithelioma.

As the cancer grows ulceration takes place, and the villi, if present, disappear. The growth penetrates the muscular wall, which becomes thickened, and it finally reaches the peritoneum, causing the bladder to become adherent to adjacent organs, some of which may eventually become involved in the disease. There is a remarkable tendency, however, of these carcinomata to remain local; which fact Watson attributes to the lack of connection of the larger lymphatic channels with the mucous membrane. The inguinal glands may occasionally be infected. The lungs and the pleura are the most frequent seats of metastatic deposits. As the carcinoma breaks down and ulcerates, the urine may become exceedingly foul, and be mixed with blood, bacteria, and fragments of tissue. As a result of the irritation thus produced the kidneys become diseased, and patients affected with this disease are said to die most frequently of pyelitis. Secondary cancer of the bladder has been observed, although it is extremely rare. In a case reported by Targett the disease was found in the muscular layer.

The most characteristic and commonest symptom of bladder-tumors is hæmaturia. The symptoms of catarrhal inflammation come later, and a microscopical examination may lead to a diagnosis of the disease. Pain is not always present, but at times the emptying of the bladder is accompanied by severe cramp. At first there is slight constitutional disturbance, but as the disease progresses there may be emaciation, and later symptoms of cachexia or of kidney complications may arise.

The *course* of the disease in isolated cases may be extraordinarily slow. Budor reports one case in which the patient died twenty-four years after the first symptoms, and Guyon reports a case of eighteen years' duration.

The *operative treatment* of cancer of the bladder consists in suprapubic or perineal cystotomy, with curetting and cautery of the growth, which is of course but a palliative measure, or in an attempt to perform a radical cure. The operation devised for this purpose consists in excision of a portion of the bladder-wall or in extirpation of the bladder. Marsh mentions five cases of resection of a portion of the bladder-wall. Of these cases, two only could be said to have recovered from the effects of the operation, one living twelve months and one living four years. Marsh also adds a sixth case of his own, which was fatal. These results show a mortality of 66 per cent., and not one radical cure.

Extirpation of the bladder has been performed in four cases, according to Watson, with three recoveries, but it does not appear that the operation was performed for cancer.

In a collection of eight cases made by Stone, four were found to have died of the operation, giving a mortality of 50 per cent. One case, in which two-thirds of the bladder was removed, lived one month, dying of "asthma." In another case, in which one-third of the bladder was removed, the wound healed in fifty-five days. Recurrence of the disease took place in six months, the patient dying at the end of a year. One patient lived four years, the disease reappearing two years after the operation. Fenwick reports nine cases of operation by twisting with forceps and cutting with scissors. In one case the disease returned in three months and the patient died. In one case the growth was removed a second time, and in another two subsequent operations were performed. Baker operated upon a woman through the vagina, cutting out the growth with scissors. Three months later the patient left the hospital in good condition.

11. Carcinoma of the Kidney.

The commonest form of cancer of the kidney is the medullary; scirrhous cancer is also seen, but less frequently. Colloid cancer of the kidney is rare. The disease is most frequently seen after middle life, but it is found also in very young children, and a few cases of congenital cancer of the kidney have been reported. The disease occurs twice or three times as often in men as in women. Among children the difference in sex is not so marked.

Cancer occurs in the kidney in an infiltrated form or as a nodular growth. In the infiltrated form the kidney is somewhat enlarged, and the cortical portion is found thickened, particularly at certain points corresponding with nodular enlargements on the surface. These points are not sharply-defined foci, but they are caused by a greater development of the disease there. They have a grayish medullary appearance on section. Under the microscope the cancer-cells are seen crowding the uriniferous tubules, which are very irregularly distended. The cancer-cells are distinguished from the normal epithelium by their large vesicular nucleus. At some points these cells can be seen in the cortical portions of the kidney, and it is probable that they develop from the epithelium of these portions of the organ as well as in the deeper structures.

The nodular cancer, which develops as a distinct nodule often separated from the rest of the kidney by a capsule, many attain a considerable size. The remainder of the kidney in such cases is flattened out against the side of the tumor. The tubules may be seen in the diseased portion, but they are much elongated and constricted. The cortical portion of the kidney is often seen still partially preserved in the periphery of the tumor.

These large tumors undergo many retrograde changes, such as fatty degeneration and necrosis; also cystic degeneration, and occasionally calcification. They are often separated into lobules by broad bands of fibrous tissue. The trabeculæ which surround the alveoli are often very delicate, and they seem to consist almost solely of blood-vessels. Such growths are necessarily highly vascular (Orth). There is occasionally seen adeno-carcinoma of the kidney strongly resembling adenoma, and this form may assume the villous type.

The lymphatic glands behind the peritoneum and in front of the spine are affected early in the disease. The results of operations upon the kidney for cancer are not encouraging. In fourteen cases of nephrectomy compiled by Gross the operation was very fatal, giving a mortality of 71.42 per cent. Death was caused either by uræmia, by shock, or by peritonitis. Of the four survivors, two died of secondary growths at the expiration, respectively, of forty-four days and two months, and the remaining two were alive at the end, respectively, of two months and thirteen months. Gross regards the disease as one which should be excluded from the category of cases for which nephrectomy should be performed. Both Butlin and Greig Smith speak unfavorably of the operation.

Fenger recently reported a case of adeno-carcinoma of the kidney the size of an egg, for which he performed lumbar nephrectomy successfully. The patient was alive and well two and a half years after operation. Fenger quotes a case of Israel who diagnosticated a carcinoma the size of a cherry and operated, obtaining a radical cure; that is, according to the three-year limit.

12. Cancer of the Testicle.

Carcinoma testis occurs in the medullary form in most cases. Scirrhous and colloid carcinomas are also occasionally seen. In no case has the disease been observed before the age of twenty. In 37 cases collected by Kocher it was found in 29 between the ages of twenty and forty. In about one-fourth of the cases the same author found that the disease followed trauma. The cancer-cells develop first in the convoluted tubes from a proliferation of the seminal cells. The tubes nearest the centre of the organ are usually the first affected, the upper portion of the testicle remaining intact or being involved later in the disease. The rete is also affected secondarily.

In the scirrhous form there is a large development of connective tissue, and sometimes of hyaline cartilage and bone. On section the growth appears as a smooth surface, on which are fibres running in various directions without any evidence of normal tissue.

Medullary carcinoma appears as a grayish nodular tumor with a slimy surface. The tumor may often be quite large, and may contain many foci of broken-down tissue, and it often attains a large size.

In many cases of cancer of the testicle there are a large number of cysts (cysto-carcinoma). Secondary growths are often felt in the iliac fossa, and the lymphatic glands are enlarged along the spine, sometimes as high as the kidneys. The skin of the scrotum may be involved in many cases. Eventually metastatic deposits occur in the liver and lungs, and with the extension of the disease cachexia becomes marked. In consequence of the enlargement of the lymphatic glands pressure may take place upon the vena cava and the feet may become œdematous. The duration of the disease appears to be about two years.

Many cases of permanent cure are reported after removal of the testis, but it is in most of the cases quite uncertain whether the disease was cancer or sarcoma.

Winiwarter found in twelve cases only one in which there was no return of the disease two years and seven months after the operation. Kocher reports six cases in which a reliable microscopic examination had been made. Of these patients all were alive and well at periods varying from one to ten and a half years.

Of the few methods of *curing cancer by medication* which have been brought forward from time to time, there are none which have stood the test of practice. In view of the interest which has been taken in Koch's method of treating tuberculosis, it may be worth while to notice a similar method of treating cancer that has been recently brought to notice by Adamkiewicz. He advances peculiar views as to the nature of cancer-cells, regarding them all as protozoa, which, though they resemble epithelium, are not epithelial cells. Implanted into the brains of rabbits, they are found to possess the power to migrate into the surrounding tissues, where some of them are destroyed and some grow and form new foci of cancer-cells. He also found that when fragments of cancer are thus implanted they produce an inflammatory reaction which does not take place when fragments of healthy tissue from the living body are substituted. If the fragments of cancer are dipped for a few minutes in a 3 per cent. solution of carbolic acid or are subjected to the action of boiling water for one or two seconds before inplantation, no inflammatory reaction takes place. Adamkiewicz concludes, therefore, that there is a toxic property in the cancer-cell, and that it is due to the action of this substance that the healthy tissues melt away before the advance of cancer.

This substance he calls "cancroin," and he obtains it in solution by treating minute fragments of cancer (cut up finely) with distilled water. The mass is then rubbed up in a mortar and filtered. A slightly opalescent and alkaline fluid is thus obtained. Such a fluid, if injected into rabbits subcutaneously, is found to act as a deadly poison. Adamkiewicz obtained a similar substance from the muscle and skin of fresh cadavers by a similar method of preparation, which substance was found to resemble closely neurin. The filtrate obtained from a watery extract of fresh cadaver tissue is a clear yellowish fluid of alkaline reaction and smelling like alkaline urine.

Cancroin injected subcutaneously into cancerous growth sets up inflammatory reaction, and it gradually produces a disappearance of the cancer. Before injection this alkaline fluid is neutralized with citric acid. A 25 per cent. watery solution is then saturated with carbolic acid and is diluted with an equal quantity of water. This preparation is called "Concentration I." Concentration II. is diluted to one-half the strength, and Concentration III. is diluted to one-quarter the strength, of No. I. The author begins with a subcutaneous injection of No. III. at some point not too remote from the growth. The results of these experiments are not sufficiently encouraging to authorize a general adoption of the method.

In a personal communication from Adamkiewicz to the writer he states that, although he has had thus far but little success with the method, he nevertheless regards it as an important advance in the treatment of cancer.

The post-operative treatment of cancer is now regarded by many surgeons as a feature in the management of every case in which an operation has been performed for malignant disease. Among the drugs most frequently used for this purpose is arsenic. Wight recommends the administration of the bromide of arsenic in doses of from $\frac{1}{40}$ to $\frac{1}{10}$ grain after meals, and the carbonate of lime before meals in 5- to 10-grain doses in the tincture of calumba. Clemens' solution is a convenient form of administering the bromide of arsenic. It may be given in doses of 2 to 3 drops three times a day after meals. Wight advises that its use should be continued for from six to twelve months. In several cases of inoperable cancer he has found the progress of the disease delayed and considerable relief to pain.

Roswell Park employs arsenic in the following combination, which contains the haloid salts of mercury, arsenic, and gold: It is administered in 10-minim doses, each of which contains $\frac{1}{15}$ of a grain of bromide of arsenic, $\frac{1}{30}$ of a grain of bromide of gold, and the $\frac{1}{100}$ of a grain of bichloride of mercury. The doses may be increased up to the physiological limit, and the use of the drug should be continued for months after the operation. It may also be given in inoperable cases. (See Appendix.)

Pyoktanin was first recommended by Mosetig-Moorhof. In his original experiments anilin trichlorate was used, but in large doses this had a poisonous effect. Pyoktanin possesses the advantage of not being poisonous to the system. His object was to attack the nuclei of the proliferating cancer-cells, and then to arrest the growth of the tumor. The affinity which the anilin dyes have for nuclei first suggested to him that this staining process might be brought about upon the living cells, and their vitality be thus impaired. The agent is injected subcutaneously, so as to come in contact with the diseased cells.

The pathogenic cells are dyed by pyoktanin in the living body. The cell-stain is not apparent at first. Mosetig accounts for the absence of coloring by the presence in the cancer-cells of a chemical substance which is able to reduce the anilin dyes in such a way that they lose their color. When the tumor has been extirpated and sections have been prepared from it for microscopical examination, exposure to the oxygen of the air brings out the blue stain.

It may be used in solutions of the strength of 1 : 1000, 1 : 500, and 1 : 300. It is probable that much stronger solutions may be used with safety. Mosetig-Moorhof has given as much as 6 grammes of a 1 : 300 solution without ill effects. The injection should be repeated every two or three days. The whole mass of the tumor should gradually become impregnated with the staining fluid. Park has seen undoubted benefit from the use of pyoktanin, although as yet in no case a cure. He gives it in solutions of the strength of 1 : 1000 to 1 : 400. He also uses methyl-blue chemically pure internally, giving it usually in connection with the extracts of nux vomica and cinchona. Meyer reports one or two cases by other observers that appear to have been cured by this treatment, but in his own experience, which has been large, there has been no cure, although great improvement has been obtained in several cases.

Mosetig-Moorhof reports a case of cancer of the gall-bladder which had been opened for gall-stone. A pencil of methyl-violet was introduced every two to four days, and 0.6 Gr. methyl-blue was given by the mouth daily. The general condition of the patient improved, the growth, a villous cancer, largely disappeared, and the incision contracted to a small fistulous opening. This surgeon reports several cases of sarcoma and carcinoma in which, although permanent cure had not been effected, there was considerable improvement in the condition of the patient. (See Appendix.)

The use of Chian turpentine, Southall's solution, or Metcalf's emulsion is occasionally followed by some improvement in the ulceration which accompanies the growth of cancer. These preparations are usually given in doses of a teaspoonful three times a day, and are continued for three months. The writer has given this remedy a thorough trial, and in but one case only, a case of cancer of the tongue, did there appear to be any result whatever. In this case the ulceration in the mouth healed, but the progress of the disease continued as before.

Although the therapeutic results of the treatment of cancer are most discouraging, the disease is not one in which the patient should be abandoned hopelessly to his fate. Both mental and physical relief has been obtained by the measures already mentioned: much may also be accomplished by general measures. Park recommends efforts to improve elimination in every possible way from the skin, kidneys and the alimentary canal.

In cases of internal cancer the utmost care should be given to the condition of the digestive organs, and special rules should be laid down for the management of cases according to the locality in which the disease is situated.

XXX. SARCOMA.

The term "sarcoma," derived from σάρξ (flesh), was first used to denote all kinds of fleshy growths. There was also supposed to be a resemblance between the fibre of sarcoma—particularly of certain forms—and the fibre of muscular tissue. This group of tumors is composed of the embryonic types of connective tissue, and in this respect it differs from most other tumors, which correspond in their structure to the fully-developed tissues of the body. Its embryonic nature is shown in the large numbers of cells of which it is composed. These cells vary greatly in their character in different varieties of sarcoma, but they are all types found in embryonic connective tissue. The round- and spindle-shaped cells are found not only in these tumors, but also in certain stages of development of fœtal tissue, and also at certain periods in the process of repair in a healing wound. The giant-cell is also characteristic of the embryonic structure of the medulla of bone, and it is seen both in bone and in connective tissue during that period of a morbid process when the embryonic type reasserts itself. There is this important difference, however, between the cells of inflammation and repair and those of sarcoma: in that the former have but a temporary existence, whereas the latter tend to indefinite growth; it is this tendency which gives to sarcoma its malignant character.

These cells are characteristic not only in their shape, but also in their disposition in an intercellular substance, as is the case with all cells of the group of connective substances. This intercellular substance may at times be very scanty and difficult to see, and it is then composed either of delicate fibres or of granular material; at other times it may be more distinctly fibrous. It may also be composed of a transparent mucous substance, such as is found in the fœtal cord. Occasionally it forms between the cells a delicate network which resembles the reticulum of the lymphatic glands. As the intercellular substance increases in quantity the cells diminish in number, and with this change is found a corresponding diminution in the malignancy of the growth.

By adhering very strictly to these lines in deciding upon the microscopic diagnosis of sarcoma the surgeon is not likely to mistake it for a tumor arising from a different form of tissue, such as carcinoma, wherein the epithelial cells are in direct contact with one another, being cemented together, and are enclosed in alveolar spaces by the stroma. The combined forms of sarcoma and carcinoma mentioned by Virchow are, in the light of these distinctions, no longer recognized. These growths originate from different germinal layers in the embryo, and they remain for ever after distinct. The endothelial growths in this respect come nearer to sarcoma, and they are so classified by some authors, although they have been placed among the carcinomata.

Sarcoma is usually a very vascular tumor, and in some cases the blood-vessels are developed to such a degree that the tumor actually pulsates. Microscopically, the walls of the vessel appear intimately connected with the new growth, and many of the walls seem to be made up almost solely of cells, being in many cases simply blood-spaces in the centre of the growth. Interesting in this connection is a growth regarded by some observers as allied to sarcoma, and described by Billroth as *cylindroma*, which is composed of columnar masses of endothelial cells in a more or less transparent matrix, and which is supposed to be formed from a growth of the endothelium of the blood-vessels, whose walls have undergone hyaline degeneration. Sarcoma seems closely associated with the blood-vessels, except that class known as *lymphosarcoma*, which is as intimately associated with the lymphatics.

The classification and definition which Virchow laid down for the sarcomata is substantially maintained to-day, although certain tumors that were formerly placed in this category have been dropped from the list. The tumor seen in actinomycosis was at one time supposed to be sarcomatous, until eventually its true nature was detected. It is possible that future discoveries may still further limit the number of tumors which are now regarded as sarcoma.

At present little is known about the *etiology* of this class of tumors. Cohnheim's theory that these growths depend upon a disturbance in the embryonic structure from which they spring has something suggestive in it in the light of the fact that sarcoma is often seen in infancy, or that it is even congenital in the sense that it springs from moles or other growths of congenital origin. Congenital sarcoma is comparatively rare. As a rule, sarcoma appears first at a much more mature period of life. In 100 cases of sarcoma collected by Stort 56 were men and 40 were women. The ages of the majority of the cases ranged from forty to seventy years. It appears to be of traumatic origin, and it has been known to follow blows upon the testis, the mamma, and the bones, and according to Nasse trauma is more frequently the cause of sarcoma than of any other tumor. Any source of irritation may serve apparently as a cause. Sarcoma appears occasionally in scars, and it may follow chronic inflammatory processes. Hesse reports that the lungs of the cobalt-miners of Schneeberg are invariably affected with lymphosarcoma, although other people in the vicinity do not have the disease.

Recent investigations show that the so-called "organisms of a cellular nature" are found in the cells of sarcoma as well as in those of carcinoma. Pawlowsky, following a suggestion of Steinhaus, studied the cells of sarcoma, and found organisms which he regarded as sporozoa (microsporidia). These structures are seen in the protoplasm of the cells, and they contain spherical or oval spores. They react differently from the other cells to staining fluids. He traces the spore into the cell, where it is surrounded by a ring of protoplasm which forms a capsule around the multiplying spores. Eventually, the capsules burst, and the spores are set free in the intercellular substance of the tumor, whence they reach other cells. The sarcoma-cells begin to grow and to multiply under the influence of the parasite. Pawlowsky thinks it probable that in the melanotic sarcomata these parasites obtain their nourishment from the constituents of the blood, and that they stand in close relations to the hæmoglobin of the red blood-corpuscles. So far as his own experience goes, these organisms are less frequently seen in the cells of sarcoma than in those of carcinoma.

Sarcomata may grow wherever connective tissue exists, but they are more frequently seen in the skin, the fascia, the intermuscular connective tissue, the bones, the periosteum, the brain, the ovaries, and the testicle. The classification it is customary to adopt at present is that based chiefly upon the character of the cells of which the tumor is composed.

The round-cell sarcoma is composed either of small or of large cells. The *small round-cell sarcoma* consists of round cells containing but little protoplasm, and of a globular or an oval nucleus. The intercellular substance is slight in quantity, and it is granular or is faintly fibrillated. The vessels are numerous, and they have very thin walls. This tissue closely resembles that seen in granulations. Such tumors are found in the skin, the testicles, and the ovaries (Ziegler). When the intercellular substance forms a reticulum of stellate cells anastomosing by numerous prolongations, the round cells are found in large numbers in the meshes of this reticulum, and there is found an arrangement such as is present in the lymphatic glands. Such a tissue is found in lympho-sarcoma.

The *large round-cell sarcoma* is composed of cells containing an abundant protoplasm and of a large vesicular oval nucleus. These cells are so large that they look like epithelium, and the stroma is so slight that the cells appear to be in contact with one another. Running through the growth, however, are trabeculæ of connective tissue, forming alveoli from the walls of which spring the delicate fibres which run between the cells. The tissue is very vascular, containing large vessels giving off fine capillaries that penetrate the alveoli in the delicate stroma. This tumor is called "*alveolar sarcoma*" (Fig. 100). Such an arrangement of cells and stroma corresponds very closely with that found in carcinoma, and it is only by careful preparation that the difference between the two kinds of growth can be detected. If a thin section taken from an alveolar sarcoma is shaken up with water in a test-tube or is brushed with a camel's-hair pencil, many of the cells drop out and the connective-tissue stroma is made apparent. This is not a very common form of sarcoma. It is found in the cutis, the muscle, the bone, and the testicle.


FIG. 100.—Alveolar Sarcoma (oc. 3. obj. $\frac{1}{12}$ oil im.).

The *spindle-cell sarcoma* (Fig. 101), however, is the commonest form. It is composed of long spindle-cells, of varying size, closely packed together. The cells lie with their broad surfaces in contact with one another, and they are arranged in bundles running in various directions, so that in a section one sees longitudinal and cross-sections of such bundles (sarcoma fasciculatum). There is but a small amount of intercellular substance, and blood-vessels are seen in the axes of the bundles of cells. These cells are often so closely packed together that their form cannot be made out distinctly, and the nuclei seem to lie very close to one another. The grain of the tumor is, however, characteristic, and on picking the cells apart or on brushing them the spindle-cells with their long prolongations are seen. These cells are not always fusiform, but they may have several prolongations, giving them quite an irregular shape. This variety of sarcoma is usually a good deal firmer

FIG. 101.—Spindle-cell Sarcoma (oc. 3, obj. D.).

in consistency, and is less malignant, than the round-cell sarcoma. Medullary forms occur occasionally. The prognosis of these tumors depends, however, greatly upon their locality.

The *giant-cell sarcoma*, or myeloid sarcoma, is characterized by the presence of cells of a great variety of shapes and sizes, but more particularly of the giant-cell, and a mass of protoplasm containing a large number of nuclei (Fig. 102). The nuclei are large and refractive, and are usually massed near the centre of the cell, and the protoplasm is composed of a thick, finely-granular material which has a yel-

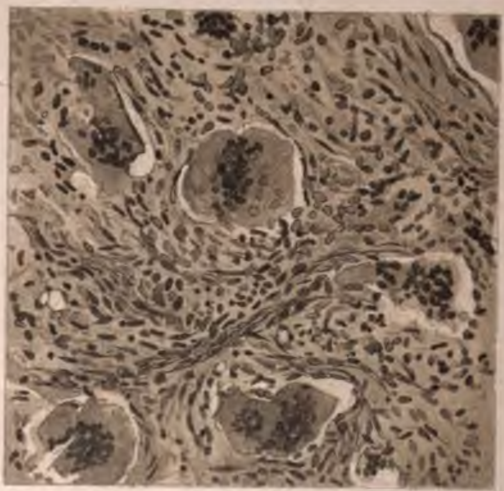

FIG. 102.—Giant-cell Sarcoma (oc. 3, obj. D.).

lowish or a brownish tinge. These cells are often quite numerous; at other times they are found only in certain portions of the growth. The other cells of which the tumor is composed are polymorphous. There are found spindle-, stellate, club-shaped, and round cells. The amount of intercellular substance is usually exceedingly small; consequently, it is a soft and pulpy tumor which often has a brownish tinge. Similar giant-cells are seen in the marrow of embryonic bone, but they are not so large. These tumors are almost always seen in the marrow of bone, but giant-cells are found also in periosteal sarcomata.

Melanosarcoma is characterized by the presence of a dark pigment in the cells. Any of the forms of sarcoma may be pigmented, but melanosarcoma usually contains round or spindle-cells. The pigment-granules are found in the body of the cells, but never in the nucleus. The pigment is arranged in many cells so as to distend the cells and alter their shape, the pigment-granules appearing as large, dark, globular masses, the clear nucleus being crowded into one corner of the cell. All the cells are not pigmented, and the younger portions of the tumor may have no pigment whatever.

These granules are not to be mistaken for blood-pigment, which, seen in "multiple-pigment sarcoma," may have been absorbed from a blood-clot the result of hemorrhage. In such a case pigment-granules are also to be found between the cells. Virchow believes that the pigment is formed in the cells, and this view is most generally accepted; others have supposed that the pigment is formed directly from the blood. These tumors grow in the choroid coat of the eye and in the skin, especially on the foot and the hand; they have also been seen in the lymphatic glands. Melanosarcoma is one of the most malignant varieties of tumor known, and metastatic deposits are found in the liver and in other internal organs, many of these metastases being unpigmented and presenting white nodules.

Sarcoma may also be classified according to the changes observed in the *intercellular substance*. When there is a large amount of fibrous stroma, which occasionally occurs in spindle-cell sarcoma, it is called a "fibrosarcoma." In *myxosarcoma* the intercellular substance is clear and homogeneous, like that seen in myxoma; the cells may be round, stellate, or fusiform. Such tumors are seen in the intermuscular septa and also in connection with sarcoma of bone. *Gliosarcoma* is a round-cell growth with an intercellular substance similar to that seen in the neuroglia. It is found in the central nervous system and also in the retina. It is a soft, white medullary growth, and is usually very malignant. *Angio-*

sarcoma has been defined as an angioma with sarcomatous growth of the vessel-wall. The sarcoma-cells form in columnar masses, apparently in the perivascular spaces, and each column of cells contains a blood-vessel in its centre. The cells have a distinctly endothelial character, which brings it close to the class of endotheliomata. These columnar masses of cells form coils which may anastomose freely with one another. The tumor may be more or less diffuse in the membranes of the brain or the peritoneum, or it may be nodular. It may be found in the brain, the nerves, the testicle, the lymphatic glands, the breast, the skin, and the bones. The tumor is very malignant, and the metastatic deposits have the same general character.

Although sarcoma seems much more isolated from the adjacent tissues than carcinoma, and it is in many cases surrounded by a sort of capsule, a histological examination shows that the cells have invaded the surrounding tissues much more deeply than the microscopic appearances would lead one to believe. The cells not only rapidly proliferate, usually by mitosis, but it is probable that many of them also possess the power of amœboid movement, and in this way detached foci may be found in the neighborhood of a tumor. For these reasons sarcoma has a strong tendency to recur locally after removal. These tumors have the power also to produce metastatic deposits, which in some cases may be so small and so numerous that the term "sarcomatosis" has been devised to express this peculiar condition. Metastasis does not occur, however, until a late period in the history of the disease, and local return of sarcoma may take place several times after operation before generalization of the growth occurs.

The metastatic growths take place along the course of the blood-vessels rather than in the lymphatics, although in the case of sarcoma of the bones the lymphatic glands may become involved. Councilman points out the closer relation of these growths to the blood-vessels, showing that it is by no means rare to find a sarcoma growing directly into a large vein, and that it may extend in this way for a long distance as a fleshy polypus moving freely in the blood-stream. As one would suppose, metastases are most commonly found in the lungs, and next in order of frequency come the spleen, the kidneys, and the liver.

Sarcoma may undergo retrograde changes during its period of growth, the most frequent being fatty degeneration of the cells. The most cellular and actively-growing sarcomata seem to possess this tendency. The sudden diminution in size or the disappearance of sarcoma as the result of treatment by arsenic or through the action of erysipelas is in many cases to be explained in this way. Mucous degeneration may also occur, and as the result of these changes cysts may develop in the tumor. Portions of the tumor often break down, owing to rupture of the softened walls of the blood-vessels; consequently extravasations of blood are frequently seen.

Sarcoma has in its early history a period during which it is far less malignant than in the later stages. During this period the tumor seems to remain stationary. The change to a more malignant growth may take place suddenly or gradually. The clinical significance of a sarcoma depends not only upon the nature of its tissue, but also upon the locality in which it is situated. The gliosarcoma, although confined to one locality, presents a condition of grave importance, owing to its relation to the central nervous system. The more rich in cells and the smaller the cells, the more rapid is the growth of the tumor.

The various localities in which the disease grows will next be studied.

1. Sarcoma of Skin.

Sarcoma of skin occurs quite frequently, although not nearly so often as cancer. It may occur primarily, but also as the result of metastasis. Sarcoma develops quite often from warts and moles, which for a long time after adult life has been reached remain unchanged, and eventually, as the result of irritation through friction or injury, change into sarcoma. It may also develop after trauma, or it may grow from granulation tissue or from a scar. Sarcoma may be congenital, and Babes reports a case of sarcoma the size of a dollar which was removed from the foot of a new-born child. The commonest period of life to see sarcoma of the skin is from thirty-five to fifty years. The disease may develop from the superficial or the deep layers of the skin or from the subcutaneous cellular tissue. In the latter case the skin is affected secondarily, and on section one can often see the sarcoma-cells pressing their way to the surface through the columnæ adiposæ.

According to Babes, many of the sarcomata of the skin spring from the walls of the blood-vessels and are of endothelial origin. According to Winiwarter, sarcomata grow from the connective-tissue structures, from the walls of the blood-vessels and lymphatic walls, and from the sheaths of the nerves. The forms generally seen here are the spindle-cell sarcoma, the myxosarcoma, the alveolar sarcoma, and the melanosarcoma. The small round-cell sarcoma is comparatively rare. The superficial form appears on the surface as a sarcomatous wart, which may eventually attain considerable size, retaining a nodulated or a papillary appearance.

The course of the disease is slow at first. There is often a period, perhaps of several years, during which the tumor bears the reputation of being benign. Then a change comes suddenly, and it is evident that the growth is sarcomatous. Even then the growth may be slow and may extend over several years. A sarcoma sometimes develops, however, with great rapidity. The adjacent portions of the skin may become affected, and eventually metastatic deposits are found in the internal organs.

Sarcoma of the subcutaneous tissue is usually more distinctly defined as to its limits, and it may attain considerable size before any metastasis takes place.

The superficial papillary sarcoma contains either round-cells or spindle-cells. It may also consist of alveolar sarcoma tissue. As it develops from some old-standing wart-like structure of the skin, it assumes a fungous growth.

Sarcomatous ulcers, seen not infrequently upon the lower extremities, contain usually a variety of cell-forms. Congenital sarcoma appears as a circumscribed, hard, round growth of doughy consistency and of a bluish color. It is either a spindle-cell sarcoma or a myxosarcoma, and it recurs rapidly after removal. The papillæ are often greatly enlarged in the affected portion of the skin (Winiwarter). Sarcoma may be multiple, and the tumors, often found in great numbers, vary considerably in size, but they are usually small. They are either subcutaneous or they infiltrate the skin, appearing as reddish nodules. They are either round-cell or alveolar sarcomas. They may also contain spindle-cells, and they are often very vascular. Death occurs from cachexia at the end of two or three years.

Melanosarcoma generally originates from a pigmented mole or it may occur in previously healthy skin. It is often found on the hands or the feet. It is not uncommon to find it springing from the sole of the foot as if it had been produced by some injury. Hutchinson describes a form of "melanotic whitlow" which appears to be connected at first with disease of the toe-nail. The nail falls off, and there is found a sarcomatous growth which later assumes a most malignant character. Pigmentation may occur in all forms of sarcoma, whether round-cell, spindle-cell, or alveolar sarcoma. The tumor when first seen may not be larger than a pea, but it may finally grow to be as large as the fist. The pigment-granules are found principally in the protoplasm of the cells, but they are seen also in the deep layers of the rete mucosum, and the pigmentation may affect the hair-follicles. The walls of the blood-vessels and the capillaries contain pigment, and pigment-granules may also be found in the subcutaneous tissue. Wickham Legg describes the case of a man fifty-four years of age in whom there was a diffuse pigmentation of the skin of the face, from which metastatic deposits eventually took place. The lymphatic glands are affected early in the disease, and all the internal organs, including the meninges, and even the brain itself, are found to contain metastatic growths. The duration of the disease seldom exceeds eighteen months to two years.

Multiple-pigment sarcoma differs from the melanosarcoma in that the pigment is apparently not obtained from the same source as in melanosarcoma, but is the result of hemorrhages which cause the deposit of blood-pigment. Some of this pigment is found in the cells and some in the intercellular substance. Microscopically, these tumors consist of small round cells or of spindle-cells, and are very vascular. The disease begins in the corium, and it later involves the papillary layer and the subcutaneous cellular tissue. In the papillæ are seen numerous extravasations of blood that have occurred as the result of laceration of the capillary walls. The walls of the vessels may also show evidences of cell-growth and pigmentation (Winiwarter). This variety of sarcoma does not originate in a pigmented mole, but is first seen on the palms or the backs of the hands or on the soles of the feet. Here the nodules occur in groups, perhaps on all four extremities, and they gradually spread toward the trunk. They begin at first as small bluish spots which are painless, but which often itch badly. Later, the nodules appear, which at first are quite small, but eventually they may increase to the size of a hen's egg. The progress of the disease is very gradual, and at the end of two or three years it may have involved the trunk and have reached the face. The whole cutaneous surface is by this time covered with nodules varying from the size of a pea to that of a hen's egg, which nodules are of a brownish or of a bluish-red color, and are more or less painful, but are rarely ulcerated. In one-fourth of the cases nodules of infiltration are found on the glans penis, the prepuce, and the scrotum. There is also a characteristic elephantiasis-like thickening of the fingers and hands and of the legs and feet, so that the fingers are stiff and distorted and the patient walks and stands only with difficulty.

The lymphatics are only moderately affected. Many of the nodules undergo retrograde changes, and after some desquamation of the epidermis over them they disappear and leave behind a dark pigmented cicatricial depression. Many undergo atrophy in the centre, while the periphery remains as an indurated wall. As the disease advances the mucous membranes become affected. Dark bluish-red patches, diffuse infiltrations, or little nodules arise on the gums, the palate, or the uvula, and the tonsils become swollen. The patients begin to have fever; bloody diarrhœa and hæmoptysis make their appearance; the liver and spleen become enlarged; and death is preceded by the symptoms of general marasmus.

Metastatic deposits are found in the lungs, the heart, the liver, the spleen, and the intestine, particularly in the descending colon (Kaposi). The age at which this disease occurs varies greatly, although the majority of cases have been of persons in middle life.

The *prognosis* is most unfavorable, although an occasional recovery is recorded. An interesting feature of the disease is the spontaneous disappearance of many of the nodules.

2. Sarcoma of Bone.

The term "osteosarcoma" is commonly used to denote sarcoma of bones, but in reality it signifies simply a sarcoma which is ossifying or which contains bone, it being used in the same way as is fibrosarcoma. It is, therefore, a term which, in this connection, should be dropped. Sarcoma of bone may in general be divided into two kinds—according to its seat in the periosteum or in the medullary tissue of the bone. The former class is called "periosteal sarcoma;" the latter, "central" or "myeloid sarcoma." The latter division shows a marked difference in histological structure, for the periosteal growths are spindle-cell tumors and the medullary growths are giant-cell sarcomata. Round-cell sarcoma is seen also both in central and in peripheral growths. Some of these tumors belong to the most malignant class of all tumors, and others are so mildly malignant that they have been supposed to be benign. According to Gross's computations, the spindle-cell form is supposed to be 43.5 per cent. more malignant than the central giant-cell sarcoma. The giant-cell form is fortunately the commonest.

Sarcomata of bone appear chiefly during the early half of life. Thus, they are seen most frequently between the ages of twenty and thirty, and they are almost as commonly met with between those of ten and twenty. Traumatism was found by Gross to be an assignable cause in fully one-half the cases he collected.

According to Nasse, in no other form of tumor is the statement of the patient so often made that some sort of an injury had previously been received. Surgeons are yet, however, entirely in the dark as to the origin of these tumors.

The *myeloid tumors* are essentially a polymorphous cell-growth, the most striking of the various cell-forms being the giant-cells, which have been referred to above. Spindle-cells and round cells are also seen. They are usually situated in the centre of the bone, but are occasionally seen in peripheral growths. One of the most frequent points of origin is the spongy tissue at the head of the tibia. They are seen also in the upper and lower jaw and in all the other long bones. In these situations they appear as soft mahogany-colored growths, which are very characteristic. For a long time they are surrounded by a shell of cortical bone, but eventually they break through at some point. They are not so vascular as might be expected from their succulent nature and from the interstitial hemorrhages to which they are so liable. They are particularly liable to fatty degeneration, and thus have a soft creamy or an amber color. They also undergo a mucoid softening, as a result of which cysts are formed containing a straw- or a buff-colored fluid. Owing to the fact that these tumors often pulsate, they are not infrequently mistaken for aneurism. They are found with about equal frequency in men and in women, and usually between the ages of twenty and thirty years. They grow more slowly than any other form of sarcoma of bone, and, as a rule, are confined to the parts in which they originate and grow; but sometimes they recur after removal, and occasionally form metastatic deposits in distant organs, principally the lungs. In 22 cases operated upon, Gross found that seventeen remained permanently well and five died of recurrence of the disease.

Central spindle-cell sarcoma is the next commonest variety. The cells may be large or small, and it is found that the small cell type is much more malignant. This form of sarcoma occurs as a smooth or slightly nodulated growth, limited by a capsule which is partly bony and partly periosteal. The cut surface is usually of a grayish-white color, and the consistence is firm and elastic. The growth is not particularly vascular, and retrograde changes are uncommon. In 16 cases Gross found two in the upper epiphysis of the tibia, five in the lower epiphysis of the femur, and two in the upper epiphysis of the humerus. The ages of the patients varied all the way from ten to sixty-eight years, the duration of life, from the beginning of the disease, averaging 37.2 months. Metastatic deposits are seen in many cases, particularly in the small-cell variety. Spontaneous fracture is met with in about one-half the cases. Pulsation is not felt frequently in this form of sarcoma.

Central round-cell sarcoma is either a simple round-cell sarcoma or an alveolar sarcoma. The latter form, which is often excessively vascular, has been regarded by some writers as a plexiform angiosarcoma. These central round-cell sarcomata are generally globular or ovoid, and are of a smooth, even outline. They are contained in a capsule which is either membranous or osseous, and from the inner surface of the capsule bands are given off which give it a lobulated appearance. The simple round-cell sarcomata are not particularly vascular, but the alveolar form is often so rich in vessels that pulsation takes place. A pulsating central sarcoma of the shaft of a long bone is almost always composed of round cells. Pulsation of the myeloid tumor at this point rarely occurs. Extensive hemorrhages may take place, and the seat of the disease may be converted into a large blood-cyst, the walls of which are composed of a thin layer of the original sarcomatous tissue. In such cases the so-called "spontaneous fracture" not unfrequently occurs. These tumors also undergo fatty or myxomatous degeneration. They grow more rapidly than any other form of tumor of bone, sometimes attaining a very large size.


FIG. 103.—Periosteal Sarcoma: amputation at the hip-joint (Warren Museum, 1517).

These growths not only infiltrate the medulla of the bone, but occasionally also invade the surrounding muscles and the ligaments of the adjacent joints. Enlargement of the neighboring lymphatic glands occurs occasionally. Gross found this enlargement to exist in only three instances. Metastatic deposits were found by him in one-third of the cases, the lungs, pleura, liver, kidneys, and osseous system being the various points invaded at different times. In one case a large vein was found filled with the sarcomatous tissue. Of 12 cases of round-cell sarcoma observed by Gross, three ran their course without amputation. Of these cases one died in six months, one in twenty-seven months, and one in thirty-eight months. Of the 9 cases in which amputation was performed, five died of the operation, one died eleven months subsequently from secondary growths in the brain and skull, and three remained well, respectively, six weeks, four months, and four and a half years after amputation.

Periosteal sarcomata are seated between the deeper layers of the periosteum and the bone (Fig. 103). The varieties are round-cell sarcoma, the spindle-cell sarcoma, osteoid or osteosarcoma, and chondrosarcoma. These forms of sarcoma occur more frequently in early life, the average age being estimated by Gross at twenty-two and one-seventh years. Giant-cells are occasionally seen in these tumors, but only to a limited degree. Fracture of the bone rarely occurs, and the tumors do not pulsate. Elevation of the local temperature is often marked. These tumors are not surrounded by a shell of bone as in the central sarcomata.

The *round-cell sarcomata* are either of the simple round-cell type or they may belong to the class of alveolar sarcoma. They are found principally on the shafts of the long bones. They are more malignant than the central sarcomata, and their growth is usually continuous and rapid. As they grow by deposits on the periphery, the bone is usually at first not affected, although it may later become involved. They appear as more or less spindle-shaped swellings, and on the cut surface they have a radiating grain or are more or less lobulated. The skin is often involved in the growth when fully developed. These tumors may recur locally, and the lymphatic glands are more frequently affected than in the case of myeloid sarcoma. In many cases the lungs contain metastatic deposits. The average duration of life is estimated by Gross at eighteen months. Of 6 cases that were successfully operated upon, only one remained well without local recurrence.

The spindle-cell sarcomata surround the epiphyses more frequently than they do the shafts of the long bones. They consequently assume more or less a pear shape. The spindle-cells vary greatly in size. While the outer layers may be rich in cells, the inner layers contain more or less fibrillated cartilaginous or bony intercellular substance. This growth, however, rarely involves the bone or the cartilage. The development of these tumors is, as a rule, uninterrupted and comparatively slow, but they appear to be almost invariably followed by metastatic deposits, and they recur frequently after operation. Their average duration of life is estimated by Gross at twenty months, or seventeen months less than the mean life of the central spindle-cell sarcomata.

Osteoid sarcomata usually occur as long pear-shaped tumors, involving the epiphysis and a portion of the shaft of the bone. They are composed of bony or calcified tissue, and of a cell-growth which is usually of the spindle-cell variety, but many also contain round cells. The bony growth radiates from the bone in the form of bony plates or spiculæ, which pursue a course perpendicular to the surface of the affected bone. The shaft is usually not involved in the disease, but at times the medullary canal may be occupied by a growth of dense bone, which may assume an ivory hardness. The outline of the shaft of the bone may still be seen on section running through the tumor.

Osteoid sarcoma, or osteosarcoma, as it grows shows a tendency to extend beyond the limiting capsule and to invade the surrounding structures. The lymphatic glands are infected in about one-fourth of the cases. Osteoid sarcomata are followed by metastatic growths in the internal organs, and are regarded by Gross as the most malignant of all forms of sarcoma of bone except the pure periosteal spindle-cell sarcoma, since 65.62 per cent. of all cases die sooner or later with metastatic deposits, whether they have been subjected to operation or not.

Chondrosarcoma resembles closely the above variety in the earlier stages of its development, the nature of the cell-growth being the same in both cases. The newly-formed cartilage is found in the deepest portions of the tumor near the bone. The radiating character of the growth is also a well-marked peculiarity. Combination of the two forms not infrequently occurs, and on section some of these tumors (which frequently reach immense size) show patches of myxomatous and sarcomatous tissue, cartilage, and bone, and they present a most striking pathological and variegated appearance.

Epulis (ἐπί, upon, οὖλον, the gum) is a name given to any growth upon the gums. The term is chiefly used, however, to denote a form of periosteal sarcoma. An epulis may contain round cells, but it is more frequently of the spindle-cell variety, and the growth is characterized by the presence of giant-cells, usually in large numbers. For this reason, and for the reason also that the bone is often involved, some writers have undertaken to describe a central as well as a periosteal form. It is, however, periosteal in its origin, but inasmuch as the growth may spring from the periosteum of the alveolar process, the bone may become affected by the time the growth has pushed aside the tooth and made its appearance. As the tumor grows the bone becomes softened and eroded, and the whole thickness of the alveolar process, and even the medullary portion of the bone, may become involved. Virchow distinguishes two forms, a hard and a soft epulis. In some cases there is a large amount of fibrous tissue and very few small cells, but the giant-cells are also seen here and there between the fibres. The softer kind is quite vascular, and frequently a vessel breaks and hemorrhage takes place into the tissue of the growth, pigment-granules being left behind when the clot is absorbed. These granules are found both in and between the cells, and they give the tumor a brownish color (pigmented epulis).

This disease is one of early life, but it may appear also in middle or in old age. It is usually seen, in the early stages, between two teeth, pushing forward as a bright red lump or granulation and attached apparently to the gum, often only by a pedicle. The deeper tissues are involved, however, and the lump returns promptly after an attempt to destroy it by tying a ligature around its base, as is often done. The disease is only locally malignant, and it may return several times after operation when not enough of the surrounding tissue has been removed. It is necessary to extract the adjacent teeth and to remove that portion of the alveolar process to which the tumor is attached. In rare cases, when the tumor is small, an incision down to the periosteum around its base will enable the surgeon to peel off the periosteum with the growth, and in this way effect a cure. Sometimes a large portion of the bone of the lower or the upper jaw must be removed to prevent recurrence.

Sarcoma of the bones of the cranium occurs as a periosteal or as a myeloid sarcoma. The periosteal form grows outward principally, but it may grow inward and destroy the bone and invade the cranial cavity. The myeloid form destroys first the diploë and separates the two tables from each other, but for some time the growth remains covered by a bony capsule. Externally these tumors may become quite prominent, and eventually they break through the cutaneous coverings. Internally they push the dura before them, but they do not become so prominent in this direction. Occasionally other portions of the bone are attacked and multiple tumors are formed. The periosteal tumors are either spindle-cell or small round-cell sarcomata.

The most frequent seat of these tumors is in the parietal bone, the temporal and frontal bones coming next in order. Tumors springing from the dura mater grow principally into the cranial cavity and compress the brain. If the tumor grows from the outer layers of the dura, the bone is first absorbed, and through the hole thus made the tumor grows out, sometimes reaching a formidable size. The tumor is usually covered with a connective-tissue capsule, which consists of the outer layer of the dura that separates it from the cranial bone. Sometimes the growth behaves more like an ordinary periosteal sarcoma, and it becomes intimately connected with the bone from the beginning. Sarcoma of the dura is usually a spindle-cell sarcoma. Its most frequent seat is beneath the parietal bone. It attacks principally individuals of middle or of late life.

J. C. Warren describes a "fungoid tumor" growing from the dura and forming a large growth on the right temple of a young lady who applied for treatment in 1846. The tumor was cut away close to the bone, and the dura was cauterized and the wound healed. Five years later she consulted Mason Warren for a return of the growth, which was quite small. No operation was advised. In 1866 she was heard from in good health. The tumor had slowly enlarged until three years previously, and it since had undergone no material change.

Other cases of slow growth of these tumors are recorded: one of twenty years', one of fifteen years', and several of four or five years' duration.

3. Sarcoma of Kidney.

Primary sarcoma of the kidney is not common, and it is most frequently seen in infancy or in childhood, whereas cancer of the kidney at this period of life is extremely rare. Many of these growths are congenital, and are discovered at or soon after birth. Sarcoma of the kidney is generally a very soft medullary growth composed of round or spindle-cells and also of stellate cells. In some portions of the tumor may be found fibrous or myxomatous tissue. The tumors attain at times considerable size, which may exceed that of a man's head. These large tumors are filled with fatty degenerated necrotic or hemorrhagic portions and cysts.

True cysts with an epithelial lining are rare. Remains of the kidney structure may be found in the peripheral portion of the tumor. The capsule is generally preserved, as are also the adrenal glands. The renal tubules and pelvis may generally also be found. The sarcoma appears to develop in the inner portion of the organ. The renal vein, and even the vena cava, may be invaded by a mass of sarcomatous tissue. The lymphatic glands are eventually affected, and secondary deposits may be found in the other viscera. In a large number of sarcomata of the kidney both striped and unstriped muscular fibre are found (myxosarcoma). The presence of such structures in the tumors is regarded by many pathologists as evidence of a disturbed embryonic formation, but Orth thinks that it is possible that these muscular growths may develop from the muscular fibre of the urinary tract. Such tumors are usually perfectly encapsuled, are separable without much difficulty from the surrounding tissues, and are not associated with involvement of the lymphatic glands or with secondary growths in any other part of the body. The disease is limited to one kidney.

Angiosarcoma may be found in the kidney, although it is an extremely rare growth. The kidneys may be the seat of metastatic sarcoma, and also of lymphosarcoma, nodules of which are seen also in the lymphatic glands. Gross collected in 1885 the statistics of 33 cases of nephrectomy for sarcoma of the kidney. The mortality of the operation was 57.57 per cent. Of the fourteen survivors, five were known to have died of metastases at periods varying from five to eighteen months; five were alive and well at the end, respectively, of seventeen, twenty-two, twenty-three, and thirty-five months, and five years. Of the 33 cases, sixteen were children under seven years of age; of these, seven survived the operation. Of these seven, one was living at the end of four months, and the others died of recurrence in five, six, nine, and eighteen months, respectively. In one of the cases that died secondary deposits were found in other organs. An analysis of the adult cases shows that seven of the seventeen recovered, and five were well at the end of thirty-one and a half months, on an average. From these data Gross concludes that nephrectomy for sarcoma in children should not be performed, but that in adults it is eminently justifiable, as it apparently cures 29.41 per cent. of the cases.

4. Sarcoma of Bladder.

Sarcoma of the bladder is an extremely rare affection. The disease is seen more often in childhood or in youth than at other periods of life. Hinterstoiser in a collection of 20 cases of sarcoma of the bladder found five in persons under twenty years of age. There were six cases, however, between the ages of fifty and sixty. The disease occurs more frequently in males than in females, thirteen of these cases being males. Some of the tumors are round-cell sarcomata, and they bear a close resemblance to the lympho-sarcomata; some have spindle-cells, and in some there is a mixture of the two kinds of cells. Myxosarcomata are occasionally seen, in such cases unstriped muscular cells being found mingled with the sarcoma-cells. Chondrosarcoma is seen in connection with polypoid growths (Orth). In a collection of 20 cases of tumor of the bladder by Sir Henry Thompson the writer finds one stated by him to be probably sarcoma, one which was probably myxosarcoma, and one which was probably round-cell sarcoma. Winckel reports a remarkable case of round- and spindle-cell sarcoma of the bladder in a girl three years of age. The tumor sprang from the anterior wall of the bladder, by the contraction of which it was forced into the urethra, whence it pushed its way into the vagina, distended this, and even dilated the os uteri.

In 88 cases of tumor of the bladder collected by Albarran, sixty-eight were carcinoma, three were sarcoma, and seventeen were benign tumors. Secondary sarcoma is occasionally found in the bladder. Fenwick in an examination of 600 cases of tumor of the bladder found but five that were really secondary (direct extension of a tumor into the bladder not being included), and of these four were sarcoma. Cabot reports a case of tumor of the prostate and bladder seen secondary to sarcoma of the testis.

5. Sarcoma of Uterus.

Sarcoma of the uterus springs from the mucous membrane or from the body of the uterus. In the latter case sarcoma-growths seem to be developed from a previously existing fibromyoma. In both forms round cells are found, but in the sarcoma of the body of the uterus may also be seen spindle-cells. Many observers have reported the presence of giant-cells.

Sarcoma of the mucous membrane appears earlier in life than carcinoma, sometimes even before puberty, and comparatively often in women who have not borne children. It is situated generally in the body of the uterus and rarely in the cervix. Lobulated or polypoid growths are usually developed, and the surface may become ulcerated. In both cases there is considerable hypertrophy of the uterus-wall, which becomes infiltrated by the new growth. When the wall has been perforated the disease attacks the peritoneum and the intestines through the adhesions which have been made, and it even attacks the abdominal walls. Polypoid papillary or cauliflower growths which are distinctly sarcomatous may occur in the cervical canal or at the os. Combinations of leiomyoma and rhabdomyoma, or tumors containing unstriped or striped muscular fibre, may be observed in these growths, and Orth reports a case in which both forms of muscular fibre were observed.

The mural sarcomata or fibrosarcomata are found in the wall of the uterus, and chiefly in the body rather than in the cervix. They are combined with muscular cells, the sarcomatous cells usually being situated at the centre of the growth, as if a fibromyoma had undergone a sarcomatous change. These tumors resemble more or less, in their coarse appearance, the uterine fibroids, and they are often found in the interior of the uterus as a polypoid tumor (Orth).

In some cases these sarcomata appear not as isolated growths, but as infiltrations of the uterine wall. They are chiefly composed of round cells, and they are often soft and medullary. Some of the uterine sarcomata may attain immense size. Gusserow reports the case of a woman fifty-one years of age with a sarcoma the size of a child's head, which tumor, on being expelled from the uterine cavity, proved to be a round-cell sarcoma. Some of the sarcomata are exceedingly vascular, and they resemble angiosarcoma. Others closely resemble carcinoma, but they are probably endothelioma.

Metastatic deposits are not often found, and less frequently in the diffuse forms. The retroperitoneal glands may be affected, and metastases may be found in the lungs, the liver, the pleura, and the adjacent organs, and the bladder and vagina may be affected by direct extension of the disease.

As the disease progresses cachexia becomes very marked, and death usually occurs from peritonitis, pyæmia, or intestinal obstruction. The progress of the disease is slow, many cases having been observed in which the disease existed ten years before death. Operative interference rarely effects a cure. A few doubtful cases have been reported as permanently cured. The growth, however, usually returns after operation. In 50 cases reported by Rogivue, three appear to have been cured; in thirty-two return of the disease was known to have taken place; and in all but two cases this return occurred within a year after the operation.

6. Sarcoma of Testis.

Sarcoma of the testis is much commoner than carcinoma. It occurs during both childhood and middle life, and even in old age. It has been seen in a child five months old and in a patient seventy years old. It is occasionally observed to follow a blow, but more frequently it occurs without any known cause. It is an interesting fact from an etiological point of view that it is not infrequently seen in both testicles. Langhans has collected 15 such cases, in many of which the second testicle has been affected several months after the removal of that first diseased. Sarcoma may occur also in the testicles as a secondary disease.

Histologically considered, there are two forms of sarcoma of the testicle—the spindle-cell and the round-cell sarcoma. In the spindle-cell variety the cut surface shows a firm growth of homogeneous appearance, with a few cysts in the substance of the tumor. The spindle-cells are found lying between the seminal ducts, which are often quite well preserved. The round-cell sarcoma may be a large- or a small-cell growth, and it may even contain giant-cells. Alveolar sarcoma is not infrequently seen. Many of the small-cell sarcomata probably belong to the lympho-sarcomata. It is this variety which is most liable to attack both testicles and which is most malignant. Cartilage, myxomatous tissue, and unstriped muscular cells are sometimes found in sarcoma of the testis. The round-cell variety is seen more often in children. Occasionally the disease assumes the form of an angiosarcoma or a plexiform sarcoma.

The disease appears to take its origin, in the majority of cases, in the posterior portion of the testicle or in the epididymis and cord. Kocher observed three cases in which the disease began in the epididymis. If the testis is first involved, the growth enlarges as a nodular tumor inside the organ, which it gradually destroys. When the growth has attained considerable size the tissue of the testis is often seen spread out over the tumor in a thin layer. The epididymis retains for some time a well-defined outline on the posterior wall of the tumor. Finally the tunica albuginea becomes involved and is merged in the sarcomatous growth, and the tunica vaginalis may follow in the same way. A hydrocele, or even a hæmatocele, may occasionally develop during the course of the disease. Nodular enlargement of the cord is often observed as the disease progresses.

The disease begins as a painless enlargement of the testicle, which may exist for many years before a rapid growth takes place. It is quite difficult to make a diagnosis between sarcoma and carcinoma, and usually the microscope alone will settle the question. The lymphatic glands are frequently affected, and in well-developed cases a large abdominal tumor may be found, caused by the involvement of the retroperitoneal glands. Metastatic deposits may occur in the skin, in the lungs, in the liver, and in the brain, and occasionally in the abdominal organs.

Sarcoma of the testicles usually runs a rapid course in children, but in adults the disease may last from eight or nine months to one or two years. In the great majority of the cases, according to Kocher, the disease returns after operation, either locally or in distant organs. One or two cases of undoubted permanent cures are reported in children, and numerous cases of immunity for several years are reported in adults.

7. Sarcoma of Breast.

Sarcoma of the breast includes nearly all the various forms of sarcoma. Round-cell sarcoma appears usually as a medullary growth, and Billroth describes such a form in a girl nineteen years of age. In this case there were striated spindle-cells, showing the development of striped muscular fibre in the tumor. In a case of round-cell sarcoma of the breast which the writer examined microscopically the growth appeared to develop around the walls of the blood-vessels.

Cases of lymphosarcoma are occasionally mentioned, and also alveolar sarcoma. The great resemblance of the alveolar type of sarcoma to carcinoma has doubtless caused it to be mistaken frequently for the latter disease. Billroth reports a case of alveolar sarcoma which assumed a melanotic type. In this case pigment-moles existed on the face and back before the development of the tumor, and metastatic deposits formed soon after the removal of the breast. Giant-cell sarcoma is found also in the breast, usually as an alveolar sarcoma. It is, however, a rare form of the disease. Spindle-cell sarcoma is seen in the variety known as *cystosarcoma.* This is the commonest form of sarcoma of the breast. As a rule, these growths, with the exception of the cystosarcoma, are unattached to the gland, but they push it aside and compress it.

While the round-cell sarcomata are soft and medullary, the spindle-cell sarcomata are firm, and in places fibrous, and are dotted over with the numerous little cysts caused by a distortion of the glandular tissue of the breast. Some of these cystic tumors contain portions that are myxomatous, and cretaceous material and some bone have been found in them. The cystosarcomata often grow to enormous size. In many cases the skin over the tumor in the different forms of sarcoma becomes involved and a hernial protrusion of the growth takes place.

The commonest seat of the disease is beneath the nipple, but when it develops at the circumference of the organ it is usually in the upper and inner quadrant. The central growths are usually cystic.

Sarcoma differs markedly from carcinoma in that it is found in early life. In 60 cases collected by Gross, eight appeared between the ages of ten and twenty years; ten appeared between twenty and thirty years; twenty-three appeared between thirty and forty years; and thirteen appeared between forty and fifty years. Spindle-cell sarcoma develops earlier in life than round-cell sarcoma. The giant-cell sarcoma alluded to above appeared in the forty-second year. The rate at which these tumors grow varies greatly. The small-cell tumors develop as a rule more rapidly than spindle- or giant-cell growths.

During its progress the tumor remains mobile and free from attachments. If the skin is not perforated, it remains natural in color. When the tumor attains considerable size, which is the case in cystosarcoma, the subcutaneous veins may be enlarged, and may give to the growth a much more malignant appearance than it really has. The nipple is usually not retracted. The lymphatic glands are rarely affected, and the contrast in this respect between sarcoma and carcinoma is very striking.

In regard to the prognosis of sarcoma of the breast, Gross, with his accustomed enterprise, collected 156 cases of the disease, the data of which throw much valuable light upon this point. The reputation of sarcoma in this situation had been that of a comparatively benign tumor. The growth was supposed to show a decided tendency to recur after operation, but the generalization of such growths was supposed to be comparatively rare. The local infection of structures adjacent to the mammary gland is indeed exceedingly rare, but Gross found metastasis to be much commoner than was supposed to be the case. The prognosis appears to be influenced materially by the age of the patient and by the size and the rate of increase of the tumor. Before the age of thirty-five, when the mammary gland is functionally most active, a small, slowly-growing sarcoma does not return; but a rapidly-increasing tumor, especially the cystic variety, is thought by Gross to be very liable to recur. After this period the danger of metastasis increases with advancing age. "A sarcoma occurring in a functionally active breast evinces a marked disposition to recur after operation, with less disposition to metastasis, while a sarcoma of the declining breast recurs less frequently, but is generalized in a greater number of instances."

The round-cell sarcoma is said to be the most malignant, but the cystosarcoma recurs, according to Gross, in more than one-half of all the cases. The good reputation of this growth maintained by numerous writers is doubtless due to the close resemblance of sarcoma to fibroma of the cystic type. Notwithstanding frequent recurrence, the removal of the tumors as fast as they appear seems to prolong life. Erichsen in 1859 removed the breast for a cysto-sarcoma, and operated five times for the recurrent growth between that date and 1866, the patient dying, some years after the last operation, of another disease. S. D. Gross in 1857 enucleated from the left breast a small tumor which proved to be a spindle-cell sarcoma. Between that date and 1862 the patient underwent twenty-one operations. Ten years and nine months after the last operation she was in perfect health.

According to Gross, sarcoma has a greater tendency to metastasis than has carcinoma; but this statement the writer hardly believes to be correct, for it is based upon the supposition that in carcinoma metastases are found post-mortem in only fifty per cent. of the cases. Gross estimates the average life of round-cell sarcoma at fifty-four months, of spindle-cell sarcoma at ninety months, and of giant-cell sarcoma at one hundred and eight months. It appears from an analysis of the data offered by Gross that, although sarcoma of the breast has a decidedly malignant tendency, surgical intervention prolongs life, and it probably results in permanent recovery. The patient may be considered safe from recurrence of the disease if four years have elapsed since the last operation.

8. Sarcoma of the Air-passages.

Sarcoma of the tonsil is a much more common disease than has usually been supposed. In Boston alone quite a number of operations have been performed for this affection, that of Cheever by the external method being the first recorded operation of its kind. Cases have also been reported by Homans and Richardson. An unrecorded case was operated upon successfully by Porter. The writer also had one case, not reported, the patient dying about one week after the operation. Newman mentions ten cases observed by himself, and he succeeded in collecting (1892) 52 cases of sarcoma of the tonsil. Of these, nine were stated to be round-cell sarcoma and eighteen were called "lymphosarcoma." A case examined microscopically by Gray proved to be alveolar sarcoma. The disease is stated by Butlin to attack males principally, and between the ages of twenty and sixty years. As several cases of disease of both tonsils are reported, it is probable that a certain percentage of the cases belong to the family of lymphosarcoma. Cases of spindle-cell sarcoma have been reported.

The slight enlargement of one of the tonsils usually causes the patient to present himself for treatment. There is nothing in the local appearance at this time to suggest the presence of malignant disease if the description of reported cases may be trusted. Presently the tonsil begins to grow rapidly: it projects toward the median line, and at the same time the anterior pillar of the fauces and the soft palate become reddened and infiltrated. By this time it will be found that there are other nodules than that of the original tumor. Growths may be observed below in the pharynx, and others may be felt externally in the cervical region. Glandular infection appears to occur early, and it is sometimes quite extensive. In the case upon which the writer operated a row of retropharyngeal glands on the affected side were exposed and removed.

As the disease progresses swallowing and articulation become difficult, and occasional attacks of dyspnœa are observed. Metastatic deposits have been observed in the lungs, the liver, the mesenteric glands, the intestine, and the peritoneum. Death, however, probably takes place in most cases before the disease has become generalized, owing to the exhaustion of the patient's strength by local complications. These growths have been removed through the mouth by knife, by écraseur, or by galvanocautery, and through the neck by external incision.

The prognosis of the early operations seems to have been most unsatisfactory, due probably to the fact that the nature of the malady had not been recognized sufficiently early to enable the surgeon to obtain a satisfactory result. Butlin mentions two cases in which there had been no return at the end of one and two years, respectively. Cheever says: "So far as I know, recurrence has taken place in all my cases in from four to six months. It has occurred usually in the glands of the neck—once on the palate. I believe I have now operated four times, always with temporary relief and good recoveries from the operation." Homans' case was reported well eighteen months after operation, and Richardson's case was in perfect health five years after the operation. Suffocation may be produced, not only by the growth of the tumor, but also by hemorrhage, which is a common accompaniment of malignant disease of the tonsils.

Sarcoma of the larynx is a comparatively rare disease. It is not often seen in childhood, but it is an affection of middle and advanced life. In 13 cases collected by Wasserman, two occurred between ten and nineteen years of age, two between twenty and thirty, and eight between forty and sixty. Most of the cases are found in males, at least three times as many males as females being attacked. Nearly all the varieties of sarcoma are said to be found here. Butlin mentions the spindle-cell sarcoma as the principal form, but round-cell, giant-cell, and alveolar sarcomata have been observed.

Sarcoma of the larynx generally originates in the subcutaneous tissue, grows slowly, and does not attain a very large size. It most frequently originates in the interior of the larynx, and principally upon the vocal cord or on the ventricular band, as irregular spheroidal masses, smooth, nodulated, mammillated, or even somewhat dendritic. Thence the growth may extend outward by infiltration, penetrating not only the membranous, but even the cartilaginous, framework of the larynx (Cohen). It is sometimes deeply ulcerated, like cancer, and at other times it is covered with a normal or congested mucous membrane. The epiglottis may also be the seat of sarcoma.

The glands are usually unaffected, and in this respect the prognosis of the disease is more favorable than that of carcinoma. There does not appear to be any tendency to metastasis. Death usually takes place from obstruction of the air-passage before the growth reaches a sufficient size to lead to generalization of the disease.

A number of operations for excision of the larynx for sarcoma have been performed in which the patients have been reported well one and two years after the operation, and one case has been reported as well ten years after the operation.

Sarcoma of the nasal passage is not a very rare disease. Bosworth collected forty-one cases. The round-cell and alveolar forms of sarcoma seem to be the prevailing types of growth. Fibrosarcoma and myxosarcoma are seen, and also angiosarcoma and melanosarcoma. The disease occurs as a pediculated tumor attached, with about equal frequency, to the outer and the inner wall of the nasal cavity. The average age at which the disease appears is about forty years, and it is seen about equally in males and in females. The disease does not appear to show the same malignant tendencies in the nasal passage that it does in other localities. Many of the reported cases were well without recurrence several months after the operation. The single case seen by the writer was that of an old woman from whom he removed a sarcomatous polyp with the cold wire-snare. The tumor was so large that it could not be extracted without turning back the left ala nasi. She made a good recovery, and was then lost sight of.

Nasopharyngeal polypi are often sarcomatous, although they may be examples of almost pure fibroma. These growths occur most frequently in males at about the age of puberty. They grow from the base of the skull, often originating in the retromaxillary fossa, whence they send out prolongations into the nose, the pharynx, and beneath the zygoma. The sarcomatous variety of this tumor may be a spindle-cell sarcoma or a myxosarcoma. At times it is highly vascular, and cases of death from hemorrhage have not infrequently occurred during attempts at removal. A very curious feature of this growth is that it shows a marked tendency to disappear at the period when the skeleton becomes fully ossified, although it frequently recurs before that period after operation. According to Bosworth, the disease may occur also later in life.

The writer has operated on several cases of sarcoma in this region in young men. In the first case the disease was limited to the nasopharynx and the tumor projected from the nostril. Frequent hemorrhages had much reduced the patient. The growth was removed with the galvano-cautery loop, and it proved to be a myxosarcoma. For two or three years after the operation fragments of tumor were removed by Dr. Hooper from the pharynx. Finally, one day, when the patient had been sent for to consider the question of an osteoplastic resection of the jaw, it was found that the growth had disappeared. The writer saw the patient several years later and found him in perfect health. A second patient applied with a similar growth which had surrounded the upper jaw and had appeared beneath the zygoma. The writer accordingly performed Langenbeck's osteoplastic resection of the jaw. Sending for him two or three years later, the writer found that in the mean time he had had two other operations performed—one through the jaw and one through the soft palate; a recurrence had taken place after the last operation, but the growth was then diminishing in size. The patient regarded himself as well. A third case was operated upon recently by the osteoplastic method.

Sarcoma occurs occasionally in the *soft palate* as a round-, alveolar-, spindle-cell sarcoma or myxosarcoma. Melanotic sarcoma has also been seen here. It usually begins on the side and extends across the palate. The neighboring tissues are rarely invaded. It occurs either early or late in life. It seems to have a tendency to remain encapsulated in many instances, and operations for its removal have been successful. In 17 cases operated upon death occurred in seven; in eight cases a cure was obtained (Bosworth).

Sarcoma is found also in the *pharynx*, where it is said to develop during middle life. Histologically, the disease does not differ essentially from the diseases above mentioned. It occurs most frequently in a pediculated form, and the prognosis after operation is quite favorable.

9. Sarcoma of the Digestive Tract.

Sarcoma of the stomach is a rare occurrence. Török mentions a case in which he performed resection. The patient was a female twenty-one years old. The tumor was quite firm and of the size of a fist. It proved to be a lymphosarcoma. A case of cystic sarcoma is mentioned among the cases for which a resection of the pylorus was performed by Billroth. Brodinsky reports a case of myosarcoma growing from the greater curvature of the stomach. The tumor weighed twelve pounds, and it lay between the layers of the omentum. Cavities were found in it varying in size from a walnut to a child's head. An ulcer the size of a hand was seen in the interior of the stomach at the point at which the tumor took its origin. The muscular layer of the stomach was much thickened, and a large portion of the tumor was made up of a growth of unstriped muscular fibre-cells. There were also spindle-cells. Nodules of the same character were found in the liver. This and a case of Eberth's of myosarcoma of the kidney were at the time the only reported cases of secondary myomatous growths. In Eberth's case the metastasis was in the diaphragm.

Sarcoma of the intestine is exceedingly rare. Baltzer collected fourteen cases of undoubted primary sarcoma of the intestine. They were nearly all males (92.8 per cent.), and the disease occurred chiefly between the ages of forty and fifty years. In the majority of cases the growth was reported to be a small round-cell sarcoma. The disease appeared to develop from the mucosa or the submucosa. It seems to be a peculiarity of these growths that they do not cause intestinal obstruction. In 4 cases resection of the intestine was attempted, with death in two cases. The result of the operation in the other two cases was not reported. Spindle-cell sarcoma is reported by Leichtenstern and also by Edwards.

10. Sarcoma of Brain.

Sarcoma of the brain may occur as a primary or as a secondary growth. Primary sarcoma of the brain appears either as a hard or as a soft tumor, and it is usually flat or wedge-shaped. The former variety was originally called by Virchow "fibrosarcoma," and many of the denser forms of tumors are genuine fibromata. In many cases the cells abound, particularly spindle-cells, and in some of them the intercellular substance has an almost cartilaginous hardness. These types are firm, translucent, and of a grayish or a yellowish-white color (Knapp).

The softer form may be a spindle-cell sarcoma purely or a myxosarcoma or gliosarcoma or a small round-cell sarcoma. The latter is the most malignant of the sarcomata in this region, except the melanotic form. It shows in sections a moist milky-white surface. Stellate and giant-cells are occasionally found in these growths, and many sarcomata are distinctly polymorphous in their cell-structure. Some forms are highly vascular and present appearances known as *angiosarcoma*. Sarcoma is sometimes easily separable from the surrounding cerebral tissue; in other cases it seems so continuous with the cerebral substance that it appears as a simple enlargement of the same.

Sarcoma of the brain shows a tendency to undergo fatty degeneration which may produce an appearance strongly suggestive of a gumma. It appears to develop from the pial sheaths of the vessels, and it is known to occur at all periods of life. Metastatic deposits from primary sarcoma of the brain are not reported, but occasionally multiple growths occur within the brain that appear to have originated from a single nodule. Sarcoma of the pia mater may occur in that membrane as a diffused growth of endothelial origin, which growth may spread itself over a large surface, causing a thickening of the membrane which extends inward along the pial sheaths of the vessels of the brain and the cord. Ordinary types of sarcoma and myxosarcoma may, however, develop from the pia mater.

10. LYMPHOSARCOMA.

Lymphosarcoma is a disease to which various names have been applied, as is usually the case in affections whose true nature is obscure and in those which are confounded with other allied affections. It is known also as *malignant lymphoma*, *pseudo-leukæmia*, and *Hodgkin's disease*. It may be defined as a disease characterized by an enlargement of the lymphatic glands and by the formation of lymphatic tissue in the spleen, the liver, the kidneys, the intestine, and the lungs—more rarely in other organs as a diffused infiltration of the tissues of the body—and by marked anæmia and the absence of leucocythæmia. Owing to its name, as well as to the impossibility of classifying it with any other group of tumors, it seems best to place it in the same chapter with sarcoma.

It has been customary to recognize among tumors of the lymphatic glands the enlargements due to tuberculosis, syphilis, and other infectious diseases; the enlargements due to leucocythæmia in which is a greatly increased number of white corpuscles in the blood; the multiple tumors of lymphosarcoma; and, finally, simple hypertrophy of the lymphatic glands due to some of the above causes to which the term *lymphoma* has been applied. This term, originally used when the knowledge of the etiology and classification of these various affections was much more imperfect than it is at present, must now be dropped if it is intended to apply it in any other sense than as an enlargement of a lymphatic gland, no matter what the cause, as those cases which were supposed to occupy an independent position under the name of lymphoma or lymphadenoma can now be classified under some one of the other headings.

The lymphatic tumors which are so prominent a feature of lymphosarcoma are composed of the tissue of the lymphatic glands. The lymphoid cells are found supported in a delicate reticulum. According as one or the other of these structures predominates, there will be a difference in the consistency of the tumors: a hard and a soft variety have been distinguished.

The soft lymphatic tumors are almost fluctuating, and they contain a considerable amount of fluid, which flows when the tumor is cut open. The cut surface shows a grayish-white substance equally distributed over the growth, so that there is no distinction between cortical and medullary portions. The lymph-cells are enormously increased in number (Fig. 104). The harder tumors have a yellowish color and they are dryer and tougher. The capsule is much thickened, and there are numerous fibrous bands running through the tumor. These growths very rarely spread beyond their capsules, and they do not undergo cheesy degeneration. Suppuration is known to occur, but it is extremely rare.

FIG. 104.—Retroperitoneal Lymphosarcoma, showing cells and stroma.

The disease usually begins in the cervical glands, which often become enormously enlarged. One side of the neck is chiefly affected, and a large number of glands grow and form a swelling filling out the side of the neck and causing a great deformity (Fig. 105). The glands do not run together into a single mass, but they are movable upon one another, and can be shelled out separately. The writer removed in this way as many as forty glands from the

FIG. 105.—Lymphosarcoma (Warren Museum, Sp. 4635).

neck of a boy. The axillary, inguinal, retroperitoneal, bronchial, mediastinal, and mesenteric glands become enlarged, usually in the above order (Gowers). The spleen is enlarged in the majority of cases, and in some instances it is almost the only gland affected. The tonsils, the thymus gland, the papillæ of the tongue, and the follicles of the intestinal mucous membrane are also affected. In cases described by Flexner there were very few glandular tumors, but the structure of the mucous membrane of the intestinal canal had largely been destroyed and replaced by lymphoid tissue. In one of the reported cases the mucous membrane of the duodenum was of a dead-white color: it was infiltrated uniformly with an opaque white material, and was marked here and there with small erosions and superficial ulcerations.

Sessile and polypoid tumors are sometimes found in the stomach, and a portion of the wall of this organ may be transformed into a continuous infiltrated mass of the disease. Occasionally the medullary tissue of bones may undergo a lymphoid change, and may become like the red marrow of children, but this is not always the case.

Metastases occur often in the liver and the kidneys, and also in the lungs, in which latter location they have been mistaken for tubercle. Large growths have been reported occasionally in the mediastinum. The trachea, pleura, peritoneum, heart, testicle, and ovary are also seats of the disease. In fact, there is hardly a spot in the body which may not be involved in the diseased process. The place of its origin, however, seems to be the lymphatic apparatus.

The principal symptoms in the early stages of the disease are those caused by the glandular enlargements, which are chiefly in the cervical region. Usually there is no febrile disturbance, but occasionally recurrent elevations of temperature have been reported. The blood shows diminution in the number of red corpuscles, without any increase in the number of white corpuscles, and toward the end of the disease there is marked anæmia combined with œdema and a tendency to hemorrhages. If the patient does not succumb to complications in the respiratory apparatus from pressure, death occurs from marasmus. The course of the disease is usually chronic, and it may sometimes last for years. Rarely the symptoms may be of the most acute type. Flexner reports the case of a girl eleven years of age who up to the day of her death had shown no symptoms of the disease. Death in this case was caused by cerebral hemorrhage. The lymphoid infiltrations were marked, but few glandular tumors were found.

The disease appears slightly more often in men than in women. In 100 reported cases seventy-five were males and twenty-five were females. It occurs at all ages of life, although more frequently in the early half of life. Occasionally the colon bacillus and pyogenic cocci have been found in some of the enlarged glands, but the presence of these organisms is not constant, and it seems to have been accidental. They may account for those exacerbations of temperature which are found in certain cases.

Flexner's studies lead him to believe that in this disease there is a toxic substance capable of producing profound degenerative changes in certain tissue-elements of the body. He observed certain bodies in the lymphoid tissue that possibly may belong to the kingdom of the protozoa. They are certainly foreign to the tissues in which they are found, and are not to be regarded as altered cells or as nuclei in the usual sense. They are round, oval, or slightly irregular in shape, and consist of a rim of protoplasm which stains faintly in eosine, and each cell contains a particle that stains in hæmatoxylin. The stained particles in the interior of the protoplasm are round, oval, or crescentic. These bodies are not contained within other cells. They are much smaller than the tissue-cells among which they are found, and they do not exceed one-third to one-half the size of a red blood-corpuscle. They are distributed irregularly in the diseased areas in the tissues, and an occasional organism may be seen in parts adjacent to the affected areas. They have been found in the stomach, the intestines, the liver, and the kidneys. In this connection the observations of Wagner on the peculiar disease affecting the cobalt-miners of Schneeberg are of unusual interest. All persons working in these mines for a number of years become affected with a disease of the lungs characterized by the formation of nodules, which grow slowly and often reach considerable size, metastatic deposits forming in other organs. In other localities, where the same metals are mined as in Schneeberg, the disease is unknown. It has been suggested that the disease owed its origin perhaps to the water drunk in the mines. The probable infectious nature of lymphosarcoma has also been suggested by other authors.

The only drug which has ever had any effect upon this form of sarcoma or any other form is arsenic. Fowler's solution, administered in doses reaching as high as 20 drops a day, given by the mouth and subcutaneously and as parenchymatous injections in the tumors, cured a certain number of cases of lymphosarcoma. In the case of an old man with a sarcoma of the neck the size of a small cocoanut the use of Fowler's solution produced a temporary remarkable diminution in the size of the tumor. This is the only case in which the writer has ever obtained any decided result from the use of the drug.

Some few years ago Fehleisen experimented with cultures of the erysipelas coccus, inoculating cases of sarcoma and carcinoma. Several tumors were made to disappear in this way, but after one or two fatal results had been obtained by certain experimenters the method seems to have been abandoned (p. 400).

This method has been revived by Spronk of Utrecht and Coley of New York. Coley's attention was drawn to this investigation after observing the cure of a case of inoperable sarcoma of the neck by an attack of erysipelas. Since 1891, Coley has been investigating the antagonistic action of erysipelas cultures upon malignant growths, more particularly on sarcoma. The first series of cases were ten in number (six sarcoma, four carcinoma), and they were treated by means of repeated injections of pure living bouillon cultures. In but four of these cases was actual erysipelas produced, although cultures of marked virulence were used. In two of the cases where erysipelas did occur the tumor disappeared completely —the one three years and the other two years later—and both patients are alive and in good condition at the present time. Most of the other cases showed more or less improvement.

To avoid the dangers of an attack of erysipelas, Coley experimented with the toxines alone, made with bouillon cultures sterilized by subjecting them to a temperature of 100° C. Of this fluid 1 to 3 C.c. were injected into the tumors, with the effect of producing all the symptoms of actual erysipelas; which symptoms, however, disappeared within twelve to twenty-four hours. The effect upon the tumors was similar in character, but less marked than when living cultures were used.

Cultures prepared without heat grown three weeks in bouillon, then filtered through porcelain, and preserved by the addition of thymol, were next used. The great difficulty lay in the weakness of the preparation, necessitating the injection of large doses to produce a marked reaction, without which no great decrease in the size of the tumors occurred.

Utilizing the principle that one germ frequently has the power to increase the virulence of another when associated with it—this being especially true of the bacillus prodigiosus—the toxines of this germ were prepared in a similar manner and used in conjunction with the erysipelas toxines in doses of .2 to .5 C.c. The results were satisfactory. The effect was not only to intensify greatly the reaction, but careful experiments with the toxines, singly and combined, in a large number of cases, confirmed the belief that the curative action of the erysipelas is likewise greatly enhanced by the prodigiosus.

Coley recently reported 35 cases of inoperable malignant tumors treated by these combined toxines: 24 of these cases were sarcoma, 8 carcinoma, 3 sarcoma or carcinoma. In 5 cases of sarcoma there is, according to him, a reasonable hope of permanent cure, and in most of the others there was marked improvement. All the cases were inoperable, and in all the diagnosis was confirmed clinically and microscopically by eminent surgeons and pathologists. During the past year the proportion of the toxines has greatly been improved, and the filtration method is no longer used. Better results have been obtained by utilizing the toxines contained in the dead germs as well as the soluble products, and experiment has shown that heating the cultures one hour at 58° C. is sufficient to render them sterile. Further improvement is due to Mr. B. H. Buxton, who suggested growing the two germs together in the same bouillon. (See Appendix.)

The experience of many prominent surgeons with this method of treatment has not been satisfactory. There is little doubt that it is of little if any value in the treatment of carcinoma. The fact that a considerable number of cases of sarcoma have been benefited by this treatment, and that a few have been cured, renders it desirable to experiment further in this direction.

XXXI. BENIGN TUMORS.

THE members of the group which are now about to be studied vary greatly from one another in their anatomical peculiarities, and some are quite complicated in their structure. They possess one characteristic, however, in common—in that they do not tend to recur after removal. Many of them at times show a tendency to become malignant, often after a period of prolonged quiescence, but this tendency is due to a change of anatomical structure to that resembling one of the forms of malignant tumors.

I. ADENOMA.

An adenoma is a tumor consisting of new-formed gland-tissue. Quite a number of tumors are classified as adenomata by some authors, but they are rejected by other authors, who insist that the growth must consist of a new formation of gland-tissue only; so that there is at present much confusion as to the precise place which many tumors should occupy. Many small growths contain a glandular structure which is clearly nothing more than hypertrophy of pre-existing gland-tissue, due, probably, to an inflammatory process, and they should not, therefore, be regarded as adenomata. Many of the cysts that form in glands present the appearance of a tumor, but they are simply the result of an obstruction of the gland-ducts. A classification of the pure adenomata cannot be attempted beyond the general statement that the gland-structure of which they are composed consists either of acini or of tubes, as one or the other of these component parts of a gland usually predominates in the new growth.

Adenoma is found in the breast, the skin, the mucous membranes, the kidney, and the liver. It is, in fact, quite widely distributed, although not a common form of tumor. The typical adenoma is a benign tumor, notwithstanding there are certain types of growth where the adenoma seems to merge into the carcinoma, and it has therefore been supposed that certain forms of adenoma should be regarded as malignant. These growths properly belong in the category of cancer. The criterion of a benign adenoma is the presence of the membrana propria which separates the investing epithelium from the surrounding connective tissue. Combinations with other forms of growth not infrequently occur, owing to development of the stroma of the gland-structure. There are obtained in this way forms known as *adenoma fibrosum*, *myxomatosum*, or *myxo-adenoma* and *fibro-adenoma*, as they are called by different writers. Cysto-adenoma occurs not infrequently, particularly in the breast and the ovary. Adenoma occurs both as a congenital tumor and as one developed during early life, but it may also be found occasionally during all the periods of adult life.

Pure *adenoma of the breast* is a rare growth. Gross was able to collect but eighteen examples. He describes it as an ovoid or a nodulated tumor of hard consistence, occasionally cystic, and limited by a distinct fibrous capsule. On section the surface is milky-white in color and dotted with small orifices. It is a solitary growth, and it generally originates in the upper and inner quadrant. Its development is slow, and it does not attain a large size. When examined under the microscope it is found to be composed of ducts or of acini containing an epithelium which is usually arranged in an orderly manner, closely resembling that seen in a normal gland.

The interstitial tissue of the mammary gland is often the seat of a growth that gives rise to tumors of considerable size. The gland-structure found in these tumors is always a prominent feature, but many writers regard them as belonging to the fibromata or to the myxomata, according as their tissue is fibrous or mucous in character. These tumors often attain great size, and present striking peculiarities which have attracted much attention, opinions varying greatly as to their character. They have been called by Paget "proliferous cysts," and the terms *adenocele* and *intra-canalicular papillary fibroma* have also been applied to them. They are seen most frequently in young women from fourteen to nineteen years of age, and they first appear in the upper and outer quadrant of the breast. Being surrounded by a capsule, they are more or less movable, and they appear to be situated just beneath the skin, but after removal a deep hole is left in the mammary gland, which has been cut into in many places during the operation. Occasionally they grow to immense size. These tumors are seen in elderly women, and they have taken many years, perhaps half a lifetime, to develop. A recent writer, Schimmelbusch, called these tumors "fibro-adenoma," and this name seems to the writer most appropriate, for there can be no doubt that there is a considerable new formation of gland-tissue. The cut surface is most characteristic, showing a lobulated growth dotted over with numerous small and tortuous slits. Occasionally this formation is a most complicated one, and numerous papillary growths may be turned out from cyst-like cavities. This formation is apparently due to the peculiar way in which the fibrous tissue has developed. Microscopically, there is found a fibrous tissue surrounding these glandular cavities, which are lined with a more or less columnar-shaped epithelium (Fig. 106). It is not always possible to say beforehand

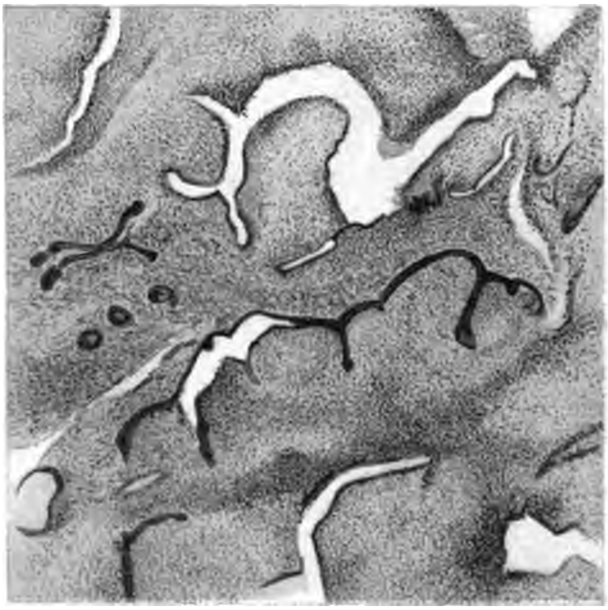

FIG. 106.—Fibro-adenoma of Breast (oc. 4, obj. A.).

whether the growth in question is or is not a benign one, as the interstitial tissue is occasionally sarcomatous (cystosarcoma). The writer has removed quite a number of such tumors, but has never observed a recurrence.

Schimmelbusch also describes as *cysto-adenoma* a diffused enlargement of the mammary glands studded with numerous small cysts containing a dark-colored fluid. Both breasts are said to be affected in the majority of cases. His description corresponds with that condition usually described as *chronic mastitis* with cyst-formation. As the epithelial structures of the gland actively participate in the growth, as may be shown by a careful microscopical examination, the growth should be regarded essentially as glandular. These cysts sometimes assume considerable size, and a breast thus affected may thoroughly be disorganized. A microscopical examination shows that there is an epithelial growth, and that the cyst-formation is caused by proliferation of the cells of the gland. The acini are increased in number—a condition resembling the changes observed during lactation. The epithelial layer is at first single, but subsequently the cells heap upon one another and dilate the acinus, and a cyst is formed by the subsequent breaking down of the cells. These tumors are found most frequently in women about forty years of age, and are benign in character.

Closely allied to this condition is that known as *diffused hypertrophy of the breast*. In one case, described and illustrated by Billroth, the coarse appearances of the growth are those of a fibro-adenoma.

The case of which the accompanying illustration is a portrait (Fig. 107) was operated upon by C. B. Porter. The following are the measurements: Right breast, largest circumference, 38 inches; length from chest-wall to nipple, 17 inches; circumference at base, 23 inches. Left breast, largest circumference, 28 inches; length from chest-wall to nipple, 14 inches; circumference at base, 23 inches. The skin was œdematous, thickened, and porky. Throughout both breasts were to be felt movable hardened masses the size of an orange. Microscopical examination showed the growth to be a diffused intracanaliclular fibroma.

A similar case recently came under the writer's care. The breasts were nearly as large as in the above case, but as the patient was several months advanced in pregnancy, it was thought best to wait and see what influence the birth of the child might have upon the growth. After the confinement the breasts diminished to less than half the former size. Amputation has been performed in many cases with success.

In the skin adenomata are found both in the sudoriparous and in the sebaceous glands. *Adenoma of the sweat-glands* is found in various parts of the body, but principally on the face, where it occurs as a small soft tumor of a dirty grayish-white color and with a nodular surface. On the cut section are seen coils of dilated ducts, from which degenerated epithelium can be pressed. At times these little tumors appear to have developed from pre-existing sweat-glands; at other times they seem to grow quite independently, one observer having found such a growth in the diploë of a cranial bone. It is a rare form of growth.

Adenoma sebaceum appears on the face in the form of papules, which are usually of congenital origin. According to Crocker, the disease is often found on the persons of epileptics, and its

FIG. 107.—Diffuse Hypertrophy of the Breast.

true nature is frequently overlooked. This variety of adenoma forms roundish, convex papules, ranging from a pin-point in size to that of a split pea; these are often bright crimson in color, and they are not infrequently associated with small fibromata, such as are seen in the "dotage" of the skin of old people.

Adenoma is found occasionally in the salivary and in the lachrymal glands. The writer has seen a very perfectly-formed adenoma in the parotid gland: it was about the size of a hen's egg, and quite soft in structure, differing markedly in this respect from the ordinary parotid tumors. Small miliary multiple adenomata are also found in the liver.

Adenoma of the kidney is found usually in the cortical substance, and it is about the size of a bean or a cherry, and often is very much smaller. It is usually yellowish or brown in color, and frequently contains small cysts which give it a porous appearance. Under the microscope are seen coils of tubules containing cells which are cylindrical in shape. There is occasionally seen a papillary variety in which the interstitial tissue forms papillary growths that project into cyst-like cavities. The epithelium is more cuboid in shape. These adenomata are often surrounded by a capsule.

Many small superficial growths in the kidney that have been supposed to be lipoma are shown by Grawitz to be fragments of accessory adrenal glands situated between lobes of kidney-tissue. The new-formed cells, like the cortical cells of the adrenal gland, contain large drops of fat. These tumors are soft and are yellowish in color, and they appear to be separated from the adjacent kidney-tissue by a capsule. They are often highly vascular and contain clots, the result of hemorrhage, which when absorbed lead to the formation of cysts: as myxomatous degeneration often takes place in them, the whole tumor may in this way be converted into a mass of débris containing fat and cholesterin. Under the microscope sections of these tumors show gland-like structures lined with polygonal cells containing fat-drops.

Adenoma of the testis is a comparatively rare growth. It is usually combined with the formation of cysts, and, in fact, the majority of cases of multilocular cysts of the testis are developed in adenomata. The tumor appears as an enlargement of the testicle. On section the new formation is found to be lobulated, and to consist of a stroma containing cysts and gland-tubes which are usually lined with a cylinder epithelium. These glandular structures do not appear to be characteristic of any particular form of gland. They are more or less dilated and tortuous canals of varying shapes and sizes. Occasionally they are filled with masses of epithelial cells heaped upon one another, giving the appearance of the epidermic clusters seen in epithelioma. The cysts do not appear as completely-closed cavities, but they communicate more or less freely with the glandular structure of the tumor.

Adenoma of the testis appears to spring from the seminal ducts by growths of the epithelium and the subjacent stroma. All cysts of the testicle do not appear, however, to be of glandular origin in this sense. Some of them seem to be the result of hemorrhage or seem to develop from dilated lymphatics, while others take their origin in embryonic remains in the testicle. When multilocular cysts have fully developed, they may, by the pressure which they exert, destroy the original growth from which they sprang, and evidence of their origin is thus lost. Some of the cysts contain a mucous fluid with gland-cells, and others have atheromatous contents containing particles of calcareous matter and pavement epithelium. There is found also cartilage in adenoma of the testicle. According to Langhans, cartilage forms in the fibrous stroma of the tumor. Striped muscular fibre has also been observed. These tumors are most frequently found between the ages of twenty and forty years. They are non-malignant, and they do not return after castration, but, inasmuch as cancer is sometimes found in combination with adenoma, removal of the testicle should always be advised.

Cyst of the epididymis is known as *spermatocele*, a condition often mistaken for hydrocele. The sac, which is usually quite large, contains a milky fluid in which are found spermatozoa. It is not developed from any glandular new-formation, but it is a a pure retention-cyst. It is a curious fact that while, in the male, cysts are found more frequently in the epididymis than in the testicle, in the female cysts are more frequent in the ovary, while parovarian cysts are less common. Spermatocele occurs most frequently in the later years of life.

Mucous polypi may contain well-marked adenomatous structures. Such glandular polypi are found in the nose, in the large intestine, and, most frequently, in the rectum. One of the most perfect types of adenoma which the writer ever examined was an adenomatous polyp removed from the rectum of a young man.

2. Goitre.

The names *goitre*, *struma*, and *bronchocele* are applied indiscriminately to all tumors of the thyroid gland, of which tumors, however, there are several distinct varieties, among them being true adenoma, which therefore deserves a place here.

Wölfler gives the following classification of thyroid tumors:

1. Hypertrophy of the thyroid gland, which is a comparatively rare disease. It may occur either at birth or at the period of puberty or of pregnancy, and it consists in a uniform increase in the normal glandular tissue, so that there are no nodules to be felt in any part of the gland. It is soft to the feel, and when vascular is compressible.

2. Fœtal adenoma, which is a formation of gland-tissue from the remains of fœtal structures in the gland. It may exist either as a single circumscribed nodule, usually firm and movable, or in numerous nodules varying in size from that of a cherry to that of an apple. It develops in both sexes at the period of puberty.

3. Gelatinous or interacinous adenoma, which consists in an enlargement of the acini by an accumulation of colloid material, and an increase in size of the interacinous tissue by a growth of round-cells (Fig 108). This form appears usually in the later periods of life, and it develops rapidly at the time of pregnancy or the change of life. At first there is a uniform enlargement of the gland, but later the different portions grow unequally and the gland presents great irregularity in shape. It is this form in which cysts are frequently found (Fig. 109).


FIG. 108.—Adenoma of Thyroid Gland.

Wölfler prefers to recognize clinically as a special variety those tumors which are highly vascular, although this condition may accompany any of the above forms. With the increase of vascularity there is frequently a visible pulsation, and a perceptible *bruit* is heard through the stethoscope. The tumor may preserve the form of the gland and have a crescentic or horse-shoe shape, or it may be circular, surrounding completely the trachea. The latter form is seen in congenital goitre, and it occasionally causes death of the new-born child by asphyxia. One lobe may enlarge and assume various shapes, or the tumor may consist of a single cyst, which in old people occasionally reaches enormous size.


FIG. 109.—Cystic Goitre.

Goitre may develop in unusual and unexpected situations in the throat, the neck, and the thorax. This mode of development is due to the displacement of portions of thyroid-gland tissue during fœtal life, and such lobes are known as *accessory* glands. According to His, the middle lobe of the gland is developed in a tract which is directly continuous with the foramen cæcum of the base of the tongue, and this tract is still frequently marked in the adult by the so-called "processus pyramidalis," a continuation of the middle lobe to the hyoid bone. It is here also that the glandulæ supra- and epi-hyoideæ are found. Such accessory glands may also be found in the vicinity of the aorta, at the base of the tongue and behind the pharynx, and in the larynx and trachea.

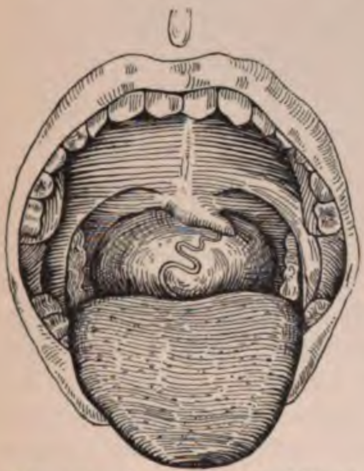

FIG. 110.—Accessory Thyroid Gland at the Base of the Tongue.

FIG. 111.—Section of Accessory Thyroid Tumor.

A tumor at the base of the tongue (Figs. 110, 111, 112) was removed by the writer from a woman fifty-two years of age. She first noticed a lump in her throat thirty-two years before, since when it slowly and steadily increased in size, and at the time of operation it was about the size of a hen's egg. It consisted of thyroid-gland tissue. No return was reported two years after the operation.

Mucous cysts are sometimes found in connection with the glandula suprahyoidea. They are lined with ciliated or pavement epithelium. Retrosternal tumors form as the result of a downward growth of thyroid tissue from the isthmus.

Goitre occurs both in man and in animals, and it appears to be independent of race. It may be either sporadic, endemic, or epidemic. Endemically, it is found in certain mountainous districts, particularly on the continent of Europe. Epidemically, it breaks out in schools and in garrisons. It occurs much more frequently

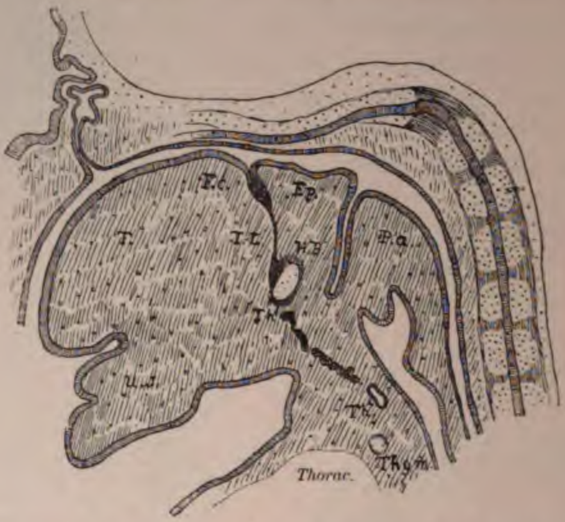

FIG. 112.—Thyreoglossal Tract (after His): *T.*, tongue; *U. J.*, under jaw; *Thorac.*, thoracic cavity; *EP.*, epiglottis; *H.B.*, hyoid bone; *F.c.*, foramen cæcum; *T.L.*, tractus lingualis; *Th. Th.*, thyroid gland; *Thym.*, thymus gland; *Pa.*, arytenoid fold.

in women than in men, and pregnancy seems to be a not infrequent cause. Whether the micro-organisms found by Klebs and Bischer in water are in reality a cause of the disease in certain cases is not yet clear. Acute infective diseases are not without their influence in the development of thyroid tumors, as they have been observed to form after malarial fever, diphtheria, and scarlet fever. Thyroid tumors usually grow extremely slowly, but occasionally an acute form is observed; this is particularly true of the vascular type. Goitre may prove fatal, owing to the effect of its growth upon the trachea, the cartilage of which undergoes degenerative changes. In this way it becomes softened, and is easily compressed or twisted on its axis by the movements of the head, as a result of which sudden death may take place.

Cysts may be treated, if small, by injection of tincture of iodine. Many cases of adenoma have been treated successfully by electrolysis. If the tumor is excised, a fragment of gland tissue about the size of an English walnut should be allowed to remain, otherwise myxœdema may develop. Closely allied to myxœdema, which may also occur idiopathically, is cretinism. Cretinism is characterized by idiocy and imperfect development of the bones, particularly marked in the skull. Cases of myxœdema have successfully been treated with thyroid juice. The mortality of thyroidectomy, which was formerly as high as 41 per cent., has, according to Bruns, dropped to 5.8 per cent. The thyroid gland may also be the seat of sarcoma and carcinoma, which are, however, comparatively rare. Round-cell sarcoma is commoner than fibrosarcoma or melanosarcoma. Both medullary and scirrhous carcinoma are observed.

It is important to say a word about the relation between ordinary goitre and that form characterized by the signs and symptoms of the so-called "Graves's disease" or "exophthalmic goitre," though the subject is so complex that only the broad outlines can be indicated. It is, in the first place, noteworthy that ordinary goitre is apt to be attended with nervous symptoms, of which tachycardia, or a tendency to palpitation, is the chief. It is a matter of great doubt what is the relation in which goitre and nervous symptoms stand to each other. Wette thinks that local nerve-irritation plays an important part, but he rather inclines to a theory which has been advanced of late (Mœbius and others) that an increased or perverted thyroid secretion, acting as a poison, has to do a good deal with the production of the symptoms of typical Graves's disease.

If the matter is looked at from another side, it will be found that Graves's disease is strongly associated with other neuropathic conditions, and that it occurs under conditions of nervous excitement. Some writers (Greenfield; Maude) believe that even when Graves's disease arises through nervous excitation thyroid-poisoning forms an important, if not a necessary, factor. This theory is not yet substantiated or even made highly probable, and the more conservative view is that the enlargement of the thyroid is on the same plane with the other symptoms in the first instance, but that it may become secondarily a source of mechanical irritation or of poisoning, or both.

Thyroidectomy has been performed more than fifty times within the past few years, mainly by German surgeons, for the relief of Graves's disease. The eventual results, on the whole, are very encouraging, but severe symptoms are apt to show themselves during the first days after operation, occasionally leading to death. It is probable that the extreme irritability of the nervous centres of these patients makes thyroidectomy a more serious operation than in cases of ordinary goitre. Putnam suggested that these symptoms may be due in part to poisoning with a thyroid secretion squeezed out during the operation and the healing of the wound.

The writer has operated upon two cases of exophthalmic goitre. In the first the temperature rose to 106° the first evening, and the pulse to 204. On removing the dressing a small quantity of thyroid juice was found upon it. The wound healed by first intention, and the patient was benefited by the operation. In the second case no bad symptoms followed the operation at first, but on the fourth day the temperature, which had been normal, suddenly rose, the pulse became extremely rapid and weak, and the patient died in a few hours. All the cases of glandular and cystic goitre which the writer has operated upon have recovered without bad symptoms, although occasionally an acceleration of the pulse has been noticed for a few days.

3. Cystoma.

Cysts of the ovary were formerly supposed to be developed from a Graafian vesicle by distention of such a cavity with fluid. Such dropsical effusion may occur to a limited extent partly as the result of inflammatory conditions. Small cysts may develop also in the corpus luteum. True cystoma is, however, epithelial in origin, and in many cases it begins as an adenoma. It is developed from an ingrowth of epithelium into the stroma of the ovary, very much in the same way that the Graafian vesicle is formed.

There are two principal varieties of *ovarian cysts:* the simple cystoma or cysto-adenoma, and the papillary cystoma. In the wall of the simple cystoma are numerous follicular depressions lined with cylinder or ciliated epithelium, and near them are small cysts lined with similar epithelium. By this ingrowth of epithelium into the wall of the cyst new cysts may be developed and the tumor may become multilocular. Parts of the tumor may distinctly be adenomatous instead of cystic. Such growths are occasionally found in the walls of large cysts or in the septum between two cysts. The papillary cystoma is characterized by the presence of a warty or papillary growth into the interior of the cyst. These growths show the greatest difference in their development. The wall of the cyst may be covered with numerous small warty tumors, or the cyst may be filled with a cauliflower mass. In rare cases the outer surface of the cyst is covered with a similar growth. There may also be an ingrowth of the epithelium into the stroma and glandular structures, thus producing a combination of adenoma with papilloma. The epithelium of the papillary cystoma is usually ciliated epithelium. Occasionally a limited metastasis is found, the peritoneum being studded with papillary growths. It has been suggested that these papillary growths may develop from the parovarium, as they are often found within the broad ligament, but it is probable that in the majority of cases they originate in the same way as the simple or glandular cystoma.

The material contained in the cysts may vary greatly in color and in consistence. It is usually of a mucous character, but it may be gelatinous. It appears to be developed from the cells that line the wall of the cyst, and it is either a product of their secretion or it may be the result of degenerative changes in the cells. The cells may undergo not only colloid degeneration, but also fatty degeneration and necrosis. Necrosis of the cyst-wall may take place, and sometimes suppuration may occur. Calcareous degeneration of the cyst-wall is also observed. It is probable that cystoma of the ovary is not of fœtal origin, but that the epithelial growths from which they are developed may begin at any period of life.

Ovarian cysts are for the most part benign, but, as has been seen, the papillary form may be accompanied by peritoneal growths. The papillary growths in the cyst may break through and appear as cauliflower excrescences on the surface, and in this way there may be a gradual metamorphosis into a carcinoma. Cysts of the broad ligament are not of new formation, but they are caused by an accumulation of secretion in the gland-tubes of the parovarium. They develop probably from the remains of the Wolffian bodies.

The ovary at times also contains cysts, which are either in part or are wholly made up of dermoid structures. These cysts may contain only dermal structures, or a great variety of tissues may be found in them, such as bone, teeth, cartilage, muscle, or mucous membrane, glands, nerves, etc. Tumors of the latter class are called "teratoma."

The commonest forms are the dermoid cysts and the simpler forms of teratoma. They are usually found on one side, but they may occur simultaneously in both ovaries. They are usually smaller than the adeno-cystoma, growing not larger than an apple at first, but they may occasionally reach the size of a man's fist or head. Several varieties can be recognized, according to the more or less complicated nature of their construction. The epidermoid cyst has a wall of connective tissue lined with epidermis, but it possesses no other attribute of the skin. The contents in this case are, distinctly, epidermic scales, which may be rolled up in firm masses or are more or less soft or soapy in appearance (Orth). The commoner form is the dermoid cyst. In this form of cyst the wall is made up of skin containing small and ill-defined papillæ, but rich in hair-follicles and sebaceous glands. Even the erector

FIG. 113.—Dermoid Cyst of Ovary, showing hair, tooth, and adipose tissue.

pili muscle and the sudoriparous gland are often found. The hair is partly free and partly rolled up into thick balls, or it is still attached to the walls. A large mass of sebaceous material is also found in these cysts (Fig. 113).

The simpler forms of teratoma are dermoid cysts containing bone and teeth. The bone appears as a series of plates in the wall of the cyst, giving to the touch the feel of an infant's head. The teeth, which are not always well formed, are arranged without order. The complicated teratoma may contain, in addition to the above-mentioned structures, cartilage and glands, such as mucous and salivary glands, mucous membrane with cylinder or ciliated epithelium, smooth and striped muscular fibre, nerves and cerebral substances, portions of eyes, fingers with nails, mammæ, etc. It is probable that these more complicated forms of cystic growth have the same origin as the cysto-adenoma of the ovary, and they result from the activity of the germinal cells (Orth).

The growth of dermoid cysts is slow, and they are generally first observed at the period of puberty, although not infrequently found in young children. Combinations of dermoid cyst with adeno-cystoma are occasionally observed, Thomson reports a case of dermoid cyst of the bladder containing hair, which cyst he removed. It was a pedunculated growth, and it was undoubtedly vesical, and not expelled from some ovarian source through the urinary passages, as sometimes occurs.

Dermoid cysts are found also in regions of the body quite remote from the ovary. The so-called "orbital wens" are true inclusion of skin of a congenital origin, as are also some of the cysts in the neck. Many of the cysts in the latter region are due to imperfect closure of the branchial clefts, and they have been called by Senn "branchial cysts." This author recognizes—1, mucous cysts; 2, atheromatous cysts; 3, serous cysts; and 4, hæmatocysts.

Many of the so-called "ranula cysts" about the base of the tongue belong to the class of mucous cysts. The atheromatous cysts are situated near the hyoid bone, and they appear as tumors bulging out from beneath the lower jaw. They do not contain hair or sebaceous material, but they are filled with an atheromatous substance containing cholesterin crystals. The cyst is of the epidermoid type.

The serous cysts correspond to what is usually known as hydrocele of the neck. These cysts are single or are multilocular, with a thin membranous wall lined with pavement epithelium. They are found anywhere in the neck, within the area of the branchial clefts, between the lower jaw and the clavicle. These branchial cysts are often found in children, but are not infrequently seen in adults also. The hæmatocysts are of the same nature, the blood mingling with the serous contents from minute hemorrhages from the cyst-walls.

4. Papilloma.

Many writers place this form of growth among the fibromata, but certain forms—particularly those seen on mucous membranes—have so marked an epithelial character that it would be incorrect to recognize the stroma as the characteristic feature of the disease. This type of the papilloma is found in the papillæ of the skin and the mucous membrane. It consists of a papilla containing a vascular connective tissue, and is covered with epithelial cells.

The connective-tissue portion of the growth may consist of a single stem or of a trunk with numerous branches. The tissue consists ordinarily of fibrillated connective tissue, and it is not infrequently infiltrated with small round cells. The vascular supply varies greatly, but in certain forms, such as the villous growth from mucous membranes, it may be very abundant. The epithelium covers each villus separately, but occasionally there may be an epithelial covering extending over several villi.

There are two forms of papilloma, the *hard* and the *soft*. The hard form occurs on the skin and the mucous membranes. The ordinary wart consists of hypertrophy of several papillæ with their epithelial coverings. It need not, therefore, strictly speaking, be called a papilloma, as there is no new formation of papillæ, but it is usually classed with these growths. The venereal wart (condyloma acuminatum) is, however, an example of a true papillomatous growth. The hard form of papilloma is found in the mucous membranes upon the lips, in the mouth, the uvula, the nasal cavity, in the larynx, the urethra, the vagina, the labia, the cervix uteri, and the bladder. It has a firm, well-developed stroma, and it is covered with layers of pavement epithelium. The soft papilloma is characterized by the formation of long, delicate, single or branched villi, the surface of which is covered with a cylinder or pavement epithelium of one or more layers in thickness. This cylinder may cover several villi, and may give to the surface of the growth a smoother appearance than is seen in the more typical velvety villous tumors. These growths may spring from one stem or they may be multiple, covering a large surface of mucous membrane. They are very vascular, and the capillaries have ampulla-like dilatations, which account for the extensive and repeated hemorrhages that are liable to occur.

The soft, villous papillomata are found in the bladder, in the stomach and intestine, particularly in the colon and duodenum (Birch-Hirschfeld), and also in the uterus. Some writers distinguish those papillomata found on the membranes of the brain from the other forms, as they are here covered with endothelium. The Pacchionian bodies are the types of this variety; they are found in the parietal region and also at the base of the brain. Springing from the dura, they may grow into the venous sinuses (Klebs). Papillomata growing on the skin and the mucous membranes may be congenital or be acquired. They appear to be the result in the latter case of chronic irritations, as catarrhal affections.

Papilloma may occur at any period of life. Watson, in a collection of 89 cases, found 59 in males and 30 in females. In the male, 21 cases occurred between the ages of sixty and seventy, and 35 between the ages of thirty and sixty. In the female, 17 occurred between thirty and forty, and 12 after forty. Papilloma may be multiple or single, sessile or pediculated. Thompson describes the hard variety as *fibro-papilloma*, and the soft form as *fimbriated* *papilloma*. He reports several cases of fibro-papillomata removed from the bladder through the median incision in the male and through the urethra in the female, all of which cases made a good recovery with permanent cure. The tendency of papilloma of the bladder to bleed is one of its most marked clinical features. Papilloma of the bladder may be combined with carcinoma, in which case characteristic epithelial cells are found in the base of the tumor in the bladder-wall.

Papillomata of the larynx occur more frequently than all other forms of benign tumors of this region. They are situated in the large majority of instances on the vocal cords, usually in the anterior portion of the larynx. In rarer cases they are found upon the ventricular bands, the ary-epiglottic folds, and the epiglottis (Bosworth). As a rule, they confine themselves to the supraglottic portion of the larynx in adult life, although in children they occasionally extend below the cords. They are usually sessile in character, though occasionally pedunculated. They may occur singly or in groups, and they vary in size from a millet-seed to a growth more or less completely filling the supraglottic laryngeal cavity. They become a growth of great clinical importance, owing to the obstruction which they offer to the air-passages. Papilloma of the soft palate and the uvula may occasionally grow to considerable size, but it does not, as a rule, give rise to serious symptoms. Newman describes a papilloma of the œsophagus situated on the anterior wall immediately behind the cricoid cartilage, which papilloma caused during life considerable obstruction to swallowing.

5. Fibroma.

Fibrous tissue occurs in nearly all tumors, and in some it forms a very considerable portion of the growth, as in the tumors already described. It occurs as a mixed form with other growths, as in myxoma, sarcoma, neuroma, etc. Fibroma occurs in two principal forms, which correspond in character with the two varieties of connective tissue found in the body—namely, the hard and the soft or areolar fibroma (Birch-Hirschfeld).

The *hard fibroma* consists of bundles of fibres closely packed together, interspersed with numerous connective-tissue corpuscles. The relation in the number of cells to the intercellular substance is characteristic of this tumor (Fig. 114). When the cells begin to exceed in number the intercellular substance, there are presented conditions approaching those found in sarcoma. A fibroma is usually a well-defined nodular growth, showing a tough tissue when cut open, and containing very few blood-vessels, and is situated principally in the subcutaneous cellular tissue, in the connective tissue of the skin, of the muscles, periosteum, nerve-sheaths, and serous membranes.

FIG. 114.—Fibroma.

Fibrous tumors occur in the interstitial tissue of organs, such as the kidney, the female breast, and in the liver, the spleen, and the ovaries. Many of the polypoid growths found on mucous membranes must be regarded as fibromata.

One of the commonest seats of fibroma is the skin. The warty growths, although largely composed of fibrous tissue, are usually classified with the papillomata. A variety which has lately excited much attention is seen in the *multiple fibromata* of the skin. They occur sometimes in enormous numbers, covering nearly the whole surface of the body, and associated with them are often pendulous tumors of considerable size. Such growths in the skin were called "fibroma molluscum" by Virchow, but V. Recklinghausen called attention to the fact that these growths take their origin from the fibrous sheaths of the nerves and the various channels, such as the sweat-ducts and the hair-follicles. In his opinion, many of these tumors should be regarded as neurofibromata. He found the papillary layer of the skin quite unaffected. In many of the cases of multiple fibroma reported it was found that tumors connected with the nerve-trunks also existed. Such was the condition found in a case reported by Payne, who, however, observed no actual connection between the fibromata of the skin and nerve-fibres. Payne explains the coexistence of nerve-fibres and skin fibroids on the supposition that, inasmuch as both the epidermis and the nervous system arise from the epiblast, these two structures have a deep-lying connection which makes them homologous parts.

Keloid (χηλή, a claw), which is a fibroma of the cutis vera, may develop spontaneously or in a scar. Two varieties are recognized —the *true* and the *false* keloid. There is, however, a tendency among writers at the present time to disregard this distinction. True keloid has always been considered as a spontaneous new formation in the corium independent of pre-existing wound. It is now supposed that true keloid may take its departure from some minute scar which has escaped notice.

The typical *true keloid* is situated over the sternum, and it appears as a raised elongated growth, frequently with claw-like prolongations at either end. Its surface is smooth and shiny, and the color red like that of a hypertrophied scar. It grows to a certain point, reaching the length of about two inches, and then remains stationary. There is no tendency to ulceration. It is an extremely rare disease, and the writer has seen but two examples. According to Hebra, it is found once in two thousand cases of skin disease. It is not painful, but it gives rise to an itching, prickling sensation. It rarely disappears, and if excised it returns promptly.

False keloid, which is a growth similar in color and consistency to true keloid, develops from a scar, no matter in what part of the body. It varies greatly in size, and it may be of any shape. A favorite seat is the lobe of the ear after puncture, and it is also found frequently on the chest-wall. It occasionally springs from acne-pustules, and in this case it is multiple. Keloid is said to be found rarely on the mucous membrane. Verneuil reports a case of keloid of the conjunctiva. Ziemssen reports the case of an individual who had one hundred and five keloids.

True keloid appears to be a disease of adult life, but false keloid may appear at any age. There seems to be a keloid disposition in certain families and individuals, and the peculiarity of the African race in this respect is well recognized. False keloid grows to a certain point, remains stationary for many years, and finally flattens somewhat and becomes paler. In negroes, although it attains unusually large size, it is said eventually to disappear entirely.

Hutchinson observed in a negro an extensive keloid growing in the cicatrix following a burn. After the keloid developed numerous small scars, which had existed before, began also to indurate.

This occurrence suggested to Hutchinson the probability that in some way the keloid patch had shed into the blood infective material which had the power of developing only scar-tissue.

FIG. 115.—True Keloid (longitudinal section).

Microscopically, the tumor, both in true and in false keloid, is found to be composed of bundles of fibres running horizontally some little distance beneath the surface of the corium and arranged parallel with the long axis of the tumor. In true keloid the papillæ with their normal covering of epidermis are seen above the growth (Fig. 115), whereas in false keloid only scar-tissue exists over the tumor. In true keloid, however, when there is considerable pressure from growth the papillæ are flattened out. The fibrous growth so characteristic of keloid can be traced to the walls of the blood-vessels in the vicinity. It is probable that the fibrous tissue develops from the outer walls of the blood-vessels, as the writer has been able to observe a round-cell growth and also fusiform cells in the adventitia. As bundles of fibres in this way form around the arteries, the tissue of the corium is gradually compressed by them, and the different bundles thus uniting form the keloid.

The origin of these tumors from the walls of blood-vessels suggests the possibility of the existence of muscular tissue at some period in the development of these growths, and it is not improbable that some forms of keloid may be classed with the fibromyomata.

One case is reported of a spontaneous growth in the face having returned, after excision, in the scar and in the points of suture, and being subsequently cured by hypodermic injections of ergot.

Pendulous tumors occur in the skin, and they sometimes attain a large size. Some of them may develop from scars; others are spontaneous growths which lie in overlapping folds. Closely allied to this group of tumors is *dermatolysis*, but this term should be applied strictly to a loose fold of skin containing no fibrous tissue.


FIG. 116.—Nasopharyngeal Fibroma (Sp. 1247-2, Warren Museum).

The enormous growths of elephantiasis depend upon the formation of a fibrous tissue similar to that seen in fibroma. It is, however, a diffuse growth, with an etiology peculiarly its own, and it is not now classed with this form of tumor.

Some forms of fibroma arise from the tissue of the periosteum. A striking example of this form of tumor is the *nasopharyngeal polyp*, which is often a pure fibroma springing from the base of the skull. When composed of fibrous tissue the polyp is a perfectly benign tumor, and it does not recur after removal. The accompanying illustration (Fig. 116) shows such a growth which had involved the nasal passage and the pharynx and had grown outward beneath the zygoma. A lobe had also penetrated the antrum and perforated the hard palate. It was therefore so intimately connected with the superior maxilla that it was decided to excise that bone. The patient, who was a boy aged fourteen, has remained well for several years since the operation.

Fibrous polyps are found also growing from the walls of the large intestine, taking their origin from the connective tissue of the submucosa. They are found occasionally also in the rectum. Another form of tumor which is occasionally fibrous is the intracanalicular papillary growth in the breast, in which case the interstitial tissue of the tumor is purely fibrous. Its association with sarcoma and myxoma is mentioned elsewhere.

The *soft fibroma* contains loose areolar connective tissue, the spaces of which are filled with serous fluid, which gives the appearance of œdematous tissue. Occasionally large cyst-like spaces are found in them. It may be found in the skin, in the subcutaneous connective tissue, in the intermuscular tissue and the periosteum, and, according to Birch-Hirschfeld, even in bone. A familiar type of this soft fibroma is the mucous polyp, which, in many cases, is purely fibrous. It has sometimes been called the "œdematous fibroid." Many of the cases of molluscum verum of the skin belong in this class.

A fibroma has a very slow growth. It may remain for a long time without any change whatever, and then suddenly take on a rapid growth. In such cases there is probably a transformation into sarcoma. Fibroma occurs in both sexes and in various races, and it may begin in early life. It often undergoes calcification and sometimes fatty metamorphosis.

6. Myxoma.

Myxoma (*μύξα*, mucus) is a tumor composed of tissue which finds its type in mucous tissue. It corresponds to the fibrocellular tumor of Paget. This tissue is found in abundance in embryonic life, and it is the structure from which adipose tissue is subsequently formed. It is seen also in the fœtal cord. In the adult it is found in the vitreous humor, and it is observed also as a degenerative change in adipose tissue and in the medulla of bones of old people.

Myxoma is closely allied, therefore, to lipoma, and indeed combinations of both structures in the same tumors are not infrequently seen. Tumors of this nature which grow from adipose tissue should therefore be considered fairly homologous. There is also a semi-homologous type in the myxomas arising from the perineurium, the neuroglia being closely allied also to the mucous tissue.

Histologically, mucous tissue is found in two forms. In one the cells are round and are imbedded in a transparent intercellular substance. In the other form the cells are long and spindle-shaped, or are stellate with long prolongations which anastomose with one another. The substance of which the matrix of the tumor is composed is mucin, which coagulates on the addition of alcohol, forming a thread-like or membranous deposit. There is a network thus formed somewhat like that seen in fibrin (Fig. 117). Myxoma may occur alone or in combination with other tissues. A pure myxoma with very few cells in it, consisting principally of transparent intercellular substance, is known as a *hyaline myxoma*. If there is a considerable amount of fibrous tissue in the intercellular substance, it is known as *myxoma fibrosum*. A very cellular type is called "myxoma medullare." Myxoma may also be combined with cartilage and adipose tissue, and at times may be

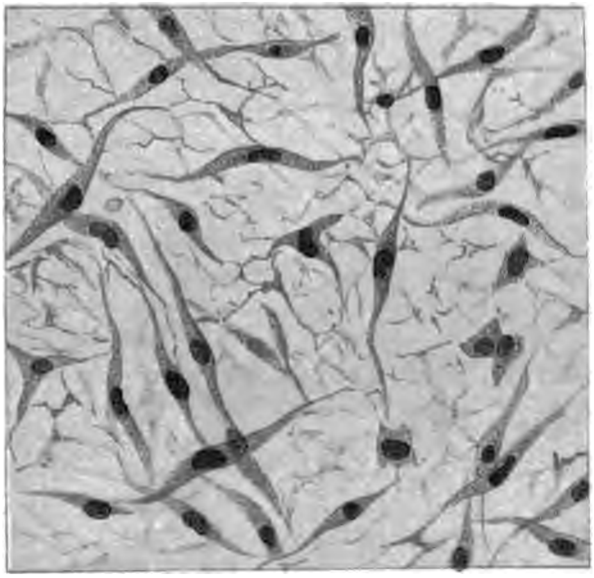

FIG. 117.—Myxoma (oc. 4, $\frac{1}{12}$ oil-im.).

very vascular. The term *myxosarcoma* is used when in sarcoma the intercellular substance is of a transparent character and contains mucin.

Myxoma occurs most frequently where there are deposits of fat or of loose connective tissue, as in the thigh, the back, the hand, and the cheeks, or at the angle of the jaw, or in the breast, the labium, or the scrotum. It is observed also in the placenta, and it is interesting to know that myxoma may occasionally develop in later life from the navel, as if it had formed from fœtal remains of the cord.

Myxoma may occur in combination with enchondroma in large tumors of the bone, taking its origin apparently from the tissue of the medulla. Myxoma occasionally attains considerable size, and it has then a well-marked lobulated structure. The writer removed one, about the size of a cocoa-nut, from the popliteal space. This tumor is occasionally found growing on the spinal arachnoid and in the ventricles of the brain, and even in the cerebral substance. The pure forms are, however, rare here. The tumor more frequently found is a myxoglioma or a myxosarcoma (Knapp). The intracanalicular papillary tumor of the breast is often myxomatous.

A not infrequent seat of myxoma is in the nerves, where it grows from the perineurium and presses the nerve-fibres apart, and develops as a spindle-shaped or a cylindrical tumor. On the mucous membranes these tumors appear in the guise of polyps, particularly in the nose. Similar polyps have been found also in the uterine cavity. Myxoma is essentially a benign tumor, although it often assumes importance, owing to its size, to the readiness with which it breaks down, and to the difficulty of removing it thoroughly in inaccessible regions. Many of the myxomata of nerves are, however, undoubtedly malignant. Virchow reported several such examples, and metastases are reported as following the development of myxoma in the labium. The possibility that myxoma may be combined with sarcoma and carcinoma should always be kept in mind.

7. LIPOMA.

A lipoma is a tumor consisting of adipose tissue. It is a soft or a moderately firm lobulated tumor, and in its structure closely resembles the subcutaneous adipose tissue, consisting of lobules of fatty issue separated by fibrous septa of greater or lesser thickness. More rarely it occurs as a smooth globular mass. Its circumference is sharply limited by a capsule which is more or less loosely attached to the surrounding parts, so that it can readily be enucleated.

The true lipoma must be distinguished from diffuse accumulations of fat in different parts of the body in the same way that fibroma is distinguished from elephantiasis. Such are the diffuse formations of adipose tissue in the mammary glands and in the abdominal walls in cases of obesity, the accumulation of fat around the kidney, or the polypoid growths on the joints (lipoma arborescens). Masses of fatty tissue occur on the fingers and toes in consequence of disease of the spinal cord, and great development of the adipose tissue occurs congenitally in the extremities in cases of gigantism. There are, however, certain diffuse forms of lipoma which deserve the name of tumors and which should be classified as such.

Microscopically, lipoma is seen to be made up of adipose tissue containing fat-cells similar to those seen in the subcutaneous tissue, but somewhat larger. It is usually developed from adipose tissue, but it also grows where no fat is found normally, as in the submucous layer of the intestine. When there is a large amount of fibrous tissue in the new growth the tumor is much firmer, and it is known as *fibrolipoma*. Another variety is known as *myxolipoma* where there is a combination of the two allied tissues. In some cases the blood-vessels are very numerous, and a form of erectile tissue may be developed. Birch-Hirschfeld describes such forms of cavernous lipoma in the subcutaneous tissue of the arms of old persons. Combinations may occur also with sarcoma and carcinoma.

The typical *circumscribed lipoma* is found in the subcutaneous cellular tissue, and it appears as a lobulated soft tumor lying beneath the skin. It is more or less movable, and the lobulated shape may readily be determined by picking up the margin of the tumor between the thumb and finger. It grows slowly, but sometimes reaches enormous size, and then assumes the shape of a pendulous tumor (Fig. 118). The skin on such tumors is coarse and hypertrophied, and sometimes is œdematous. When these huge growths are allowed to remain unoperated, the most dependent portion of the skin eventually breaks down, and there forms a deep, well-defined ulcer, which extends through the skin, but which does not involve the tumor. Hemorrhage often occurs under these circumstances, and the patient is finally driven to seek surgical relief.

FIG. 118.—Lipoma of Thigh: on the left, skin ulcerated.

The *diffuse lipoma* occurs in the neck, and it gives to the patient a peculiar and grotesque appearance (Fig. 119). It was first described by Brodie, and later by McCormack, Hutchinson, and others. It is called "fat-neck" (*Fetthals*) by Madelung. The growth begins usually as a tumor situated over the mastoid process and behind the ears. It may exist on one or both sides of the neck. Finally, it covers the back of the neck, being divided into symmetrical halves by a depression on the median line. It is sharply defined above at the superior curved line of the occipital bone, and it eventually grows around the neck, forming large folds at the side and the appearance of a "double chin" in front. In one of Madelung's cases a large lobe extended downward over the clavicle. The tumor-growth spreads downward and below the muscular fibres in some cases, and even between the larynx and the pharynx.

FIG. 119.—Diffuse Lipoma of the Neck and Abdomen.

Diffuse lipoma appears usually in individuals between thirty-five and forty-five years of age, and chiefly in men. Many of the patients are addicted to the use of alcohol, but in no case is general obesity described. The single case seen by the writer corresponded very accurately with the descriptions and portraits given by other writers. The patient was a middle-aged man and a heavy drinker. The tumor was removed at several operations, and, owing to the fact that there was no well-defined boundary to the growth, the dissection was difficult. In no case has there been any return of the growth after removal. Other forms of diffuse lipoma occur congenitally. The writer has on several occasions removed such diffused accumulations of fat from the cheeks of infants and young children.

The *situation* of circumscribed lipomata has been carefully studied by Grosch, who finds that they are most frequently situated on the neck and the shoulders and on the posterior surface of the trunk and the nates, consequently on those portions of the skin where the sudoriparous and sebaceous glands are most sparingly distributed. It is supposed that these glands rely largely upon the adipose tissue for the production of the excretion, and consequently unusual accumulations of adipose tissue are less likely to occur where they are found in large numbers. Multiple lipomata are also confined to the same localities, and they are often distributed symmetrically. Lipoma is rarely found on the head, but when so found it occurs more frequently on the face, particularly the forehead, than on the scalp. The palm of the hand and the sole of the foot are localities where it is seen less frequently than in any other part of the extremities.

Lipoma is found also in the serous membranes and in the submucous tissues of the mucous membranes. Enormous myxolipomata are often developed in the retroperitoneal space. Lipoma of the tongue has recently been observed by Rosenstirn. Lipoma is more frequently found in women than in men, and makes its appearance usually after middle life. Multiple lipomata are occasionally developed during childhood. Lipoma is a benign tumor, and it never returns after extirpation. It rarely disappears spontaneously, even though the patient becomes greatly emaciated.

8. GLIOMA.

Gliomata are tumors that develop from the neuroglia or reticular substance which supports the fibres and cells of the central nervous system. Examined under the microscope, they are found to contain a network of extremely fine glistening fibres in which numerous oval nuclei are supported at some little distance from one another. A careful examination of these nuclei shows that they belong to cells which anastomose with one another by numerous delicate prolongations. These cells closely resemble the normal cells of the neuroglia, but they are usually larger, and some contain several nuclei. It is from the cells of the neuroglia that these growths develop, and not from the nerve-cells (Ziegler). The number of cells in a glioma vary greatly. At times the cells predominate, at other times the fibrous network. The vessels are occasionally very numerous.

Glioma forms in the brain a tumor that is not easily distinguished from the surrounding cerebral substance, with which it appears to be more or less continuous. Its presence is recognized chiefly by a swelling and by a diffusion of color. In the cord the glioma appears to form around the central canal, and it often spreads out over considerable portions of the spinal cord. It is usually of a bright-gray color, and is somewhat transparent, or it is a grayish-white or grayish-red, and even of a deep-red color when highly vascular.

Gliomata are divided into hard, soft, and vascular forms. The hard form, or *fibroglioma*, which is found in the ependyma of the ventricles, is composed principally of a delicate fibrillated intercellular substance, and it is often associated with hydrocephalus. It may also occur elsewhere in the brain, and it is sometimes of almost cartilaginous hardness. It rarely attains great size. The *soft glioma* has a bluish-white color, such as is seen in hyaline cartilage, and it is sometimes hard to distinguish in alcoholic preparations from the surrounding cerebral substance, as it usually has no well-defined outline. It often grows to the size of a child's head, being usually found in the white substance of the anterior and posterior lobes of the brain. It contains generally numerous large cells. The small-cell glioma is more vascular, and is particularly liable to hemorrhage. The gliomata may also undergo fatty degeneration and softening.

Glioma is found in the retina in children. It contains both round and stellate cells. Eventually it may break through the sclerotic, and metastases may form in the orbital fat, in the diploë of the bones, and in the brain. In some cases metastatic deposits have been described in the liver, the kidneys, and the ovaries, but it is probable that these tumors belong in the group of sarcomata rather than to the gliomata.

Neuroglioma ganglionare is a growth composed of neuroglia, of ganglion-cells, and of nerve-fibres, and it may be diffused or be circumscribed. A portion of the tumor undergoes a myxomatous change occasionally, and these growths are then known as *myxoglioma*. In other cases there may be a combination with sarcoma (gliosarcoma). Glioma is rarely found in the cerebellum. When extensive degenerative changes occur in glioma it is often difficult to recognize the new formation, which is not suited to surgical interference, owing to its ill-defined outline.

The subject of *syringomyelia*, that has been so much discussed of late in neurological literature, deserves consideration in connection with the general subject of glioma. The prevalent view is that in such cases, owing to a lack of developmental differentiation, there is a growth of quasi-embryonic tissue of the spinal cord specially involving the neighborhood of the posterior commissure and the posterior gray horns. Sometimes, also, there is an imperfect closure of the posterior cleft. Eventually, this gliomatous tissue is liable to break down, giving rise to the formation of cavities which are generally lined with pieces of membrane. This condition is commonly met with in the cervical portion of the cord, but occasionally in other parts as well. It is sometimes associated with spina bifida and sometimes with hydrocephalus.

The clinical symptoms which are most characteristic are a loss of the sense of pain and of temperature in certain well-defined areas, associated with a relative preservation of the sense of touch. There is also a high degree of muscular atrophy, which usually occupies a smaller area than the sensory disorders. The disease is progressive and is not amenable to surgical treatment.

9. Chondroma.

Enchondroma, or chondroma, is a tumor which consists of cartilage. It occurs principally where cartilage is found normally—that is, on the bones and in the cartilage of the respiratory organs—but it may also be found where there is no cartilage.

Virchow divided the chondromata into two forms: those which grow from cartilage, or the ecchondromata, and those which grow independently of cartilage, or the enchondromata. The former class is, however, a small one, the great majority of cartilaginous tumors belonging to the class of enchondromata.

Enchondroma varies greatly in size. It may appear as a small round tumor or as a large lobulated growth (Fig. 120). It consists of either hyaline cartilage or of fibro-cartilage. The tumor may be in a state of mucous softening or be partially ossified. It may also be composed of osteoid tissue, such as is found in the ossifying callus between the bone and the periosteum, and it is then known as *osteoid chondroma* (Virchow).

The tumor consists not only of cartilage, but also of connective tissue, which, however, is usually small in quantity. It separates

FIG. 120.—Enchondroma of the Tibia, just below knee-joint (female; duration five years).

the cartilage into numerous lobules. At times the fibrous tissue may preponderate to such an extent that very little cartilage is seen. The cells vary greatly in size, in form, and in numbers in different tumors and even in the same tumor. At times they are so numerous as to crowd against one another and leave little intercellular substance. They may be exceedingly few in number in other growths. They are often quite large, and contain one or more nuclei and a well-marked capsule. In other cases the capsule is wanting (Fig. 121). In some forms the cells are stellate with anastomosing prolongations: in these tumors the tissue is usually soft, and it has the appearance of myxoma. The intercellular

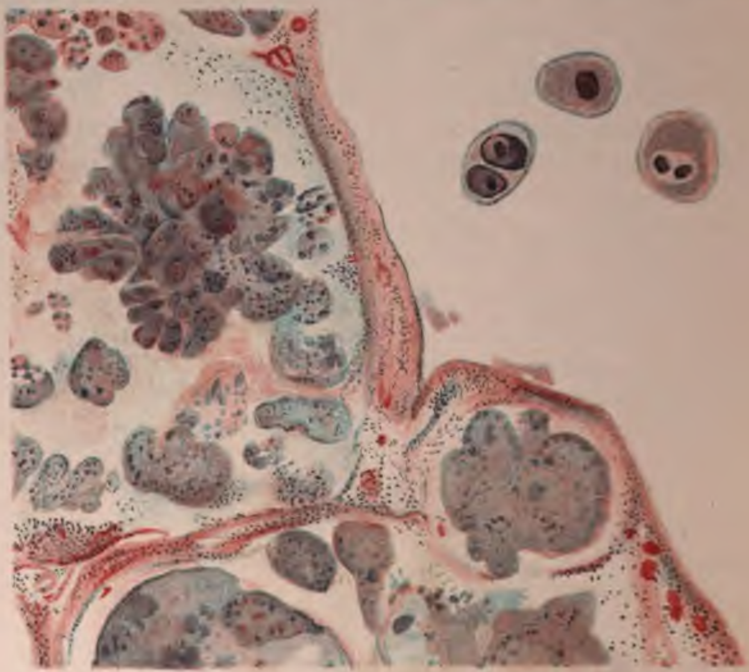

FIG. 121.—Hyaline Enchondroma (oc. 3, obj. D., and oc. 3, obj. A.; hematoxylin staining).

substance is either hyaline or fibrous. Chondroma may be combined with sarcoma.

Cartilaginous tumors may undergo a mucous softening so far as the intercellular substance is concerned, and the cells in this case undergo fatty degeneration: these changes lead to the formation of cysts. These tumors may also undergo calcification or ossification. At times chondroma may be highly vascular. Chondroma occurs most frequently during youth, at a time when the bones are developing: there is probably some connection between the formation of these tumors and irregularities in the development

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FIG. 116.—Nasopharyngeal Fibroma (Sp. 1247-2, Warren Museum).

The enormous growths of elephantiasis depend upon the formation of a fibrous tissue similar to that seen in fibroma. It is, however, a diffuse growth, with an etiology peculiarly its own, and it is not now classed with this form of tumor.

Some forms of fibroma arise from the tissue of the periosteum. A striking example of this form of tumor is the *nasopharyngeal polyp*, which is often a pure fibroma springing from the base of the skull. When composed of fibrous tissue the polyp is a perfectly benign tumor, and it does not recur after removal. The accompanying illustration (Fig. 116) shows such a growth which had involved the nasal passage and the pharynx and had grown outward beneath the zygoma. A lobe had also penetrated the antrum and perforated the hard palate. It was therefore so intimately connected with the superior maxilla that it was decided to excise that bone. The patient, who was a boy aged fourteen, has remained well for several years since the operation.

Fibrous polyps are found also growing from the walls of the large intestine, taking their origin from the connective tissue of the submucosa. They are found occasionally also in the rectum. Another form of tumor which is occasionally fibrous is the intracanalicular papillary growth in the breast, in which case the interstitial tissue of the tumor is purely fibrous. Its association with sarcoma and myxoma is mentioned elsewhere.

The *soft fibroma* contains loose areolar connective tissue, the spaces of which are filled with serous fluid, which gives the appearance of œdematous tissue. Occasionally large cyst-like spaces are found in them. It may be found in the skin, in the subcutaneous connective tissue, in the intermuscular tissue and the periosteum, and, according to Birch-Hirschfeld, even in bone. A familiar type of this soft fibroma is the mucous polyp, which, in many cases, is purely fibrous. It has sometimes been called the "œdematous fibroid." Many of the cases of molluscum verum of the skin belong in this class.

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Myxoma is closely allied, therefore, to lipoma, and indeed combinations of both structures in the same tumors are not infrequently seen. Tumors of this nature which grow from adipose tissue should therefore be considered fairly homologous. There is also a semi-homologous type in the myxomas arising from the perineurium, the neuroglia being closely allied also to the mucous tissue.

Histologically, mucous tissue is found in two forms. In one the cells are round and are imbedded in a transparent intercellular substance. In the other form the cells are long and spindle-shaped, or are stellate with long prolongations which anastomose with one another. The substance of which the matrix of the tumor is composed is mucin, which coagulates on the addition of alcohol, forming a thread-like or membranous deposit. There is a network thus formed somewhat like that seen in fibrin (Fig. 117). Myxoma may occur alone or in combination with other tissues. A pure myxoma with very few cells in it, consisting principally of transparent intercellular substance, is known as a *hyaline myxoma*. If there is a considerable amount of fibrous tissue in the intercellular substance, it is known as *myxoma fibrosum*. A very cellular type is called "myxoma medullare." Myxoma may also be combined with cartilage and adipose tissue, and at times may be

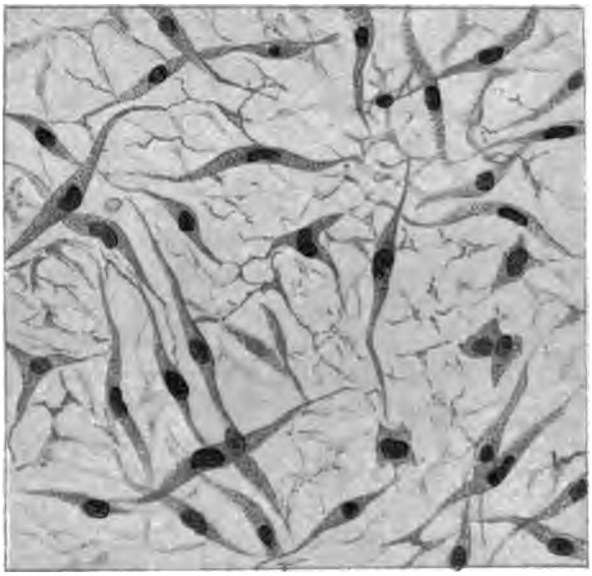

FIG. 117.—Myxoma (oc. 4, $\frac{1}{12}$ oil-im.).

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Myxoma occurs most frequently where there are deposits of fat or of loose connective tissue, as in the thigh, the back, the hand, and the cheeks, or at the angle of the jaw, or in the breast, the labium, or the scrotum. It is observed also in the placenta, and it is interesting to know that myxoma may occasionally develop in later life from the navel, as if it had formed from fœtal remains of the cord.

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A not infrequent seat of myxoma is in the nerves, where it grows from the perineurium and presses the nerve-fibres apart, and develops as a spindle-shaped or a cylindrical tumor. On the mucous membranes these tumors appear in the guise of polyps, particularly in the nose. Similar polyps have been found also in the uterine cavity. Myxoma is essentially a benign tumor, although it often assumes importance, owing to its size, to the readiness with which it breaks down, and to the difficulty of removing it thoroughly in inaccessible regions. Many of the myxomata of nerves are, however, undoubtedly malignant. Virchow reported several such examples, and metastases are reported as following the development of myxoma in the labium. The possibility that myxoma may be combined with sarcoma and carcinoma should always be kept in mind.

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The true lipoma must be distinguished from diffuse accumulations of fat in different parts of the body in the same way that fibroma is distinguished from elephantiasis. Such are the diffuse formations of adipose tissue in the mammary glands and in the abdominal walls in cases of obesity, the accumulation of fat around the kidney, or the polypoid growths on the joints (lipoma arborescens). Masses of fatty tissue occur on the fingers and toes in consequence of disease of the spinal cord, and great development of the adipose tissue occurs congenitally in the extremities in cases of gigantism. There are, however, certain diffuse forms of lipoma which deserve the name of tumors and which should be classified as such.

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FIG. 118.—Lipoma of Thigh: on the left, skin ulcerated.

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Gliomata are tumors that develop from the neuroglia or reticular substance which supports the fibres and cells of the central nervous system. Examined under the microscope, they are found to contain a network of extremely fine glistening fibres in which numerous oval nuclei are supported at some little distance from one another. A careful examination of these nuclei shows that they belong to cells which anastomose with one another by numerous delicate prolongations. These cells closely resemble the normal cells of the neuroglia, but they are usually larger, and some contain several nuclei. It is from the cells of the neuroglia that these growths develop, and not from the nerve-cells (Ziegler). The number of cells in a glioma vary greatly. At times the cells predominate, at other times the fibrous network. The vessels are occasionally very numerous.

Glioma forms in the brain a tumor that is not easily distinguished from the surrounding cerebral substance, with which it appears to be more or less continuous. Its presence is recognized chiefly by a swelling and by a diffusion of color. In the cord the glioma appears to form around the central canal, and it often spreads out over considerable portions of the spinal cord. It is usually of a bright-gray color, and is somewhat transparent, or it is a grayish-white or grayish-red, and even of a deep-red color when highly vascular.

Gliomata are divided into hard, soft, and vascular forms. The hard form, or *fibroglioma*, which is found in the ependyma of the ventricles, is composed principally of a delicate fibrillated intercellular substance, and it is often associated with hydrocephalus. It may also occur elsewhere in the brain, and it is sometimes of almost cartilaginous hardness. It rarely attains great size. The *soft glioma* has a bluish-white color, such as is seen in hyaline cartilage, and it is sometimes hard to distinguish in alcoholic preparations from the surrounding cerebral substance, as it usually has no well-defined outline. It often grows to the size of a child's head, being usually found in the white substance of the anterior and posterior lobes of the brain. It contains generally numerous large cells. The small-cell glioma is more vascular, and is particularly liable to hemorrhage. The gliomata may also undergo fatty degeneration and softening.

Glioma is found in the retina in children. It contains both round and stellate cells. Eventually it may break through the sclerotic, and metastases may form in the orbital fat, in the diploë of the bones, and in the brain. In some cases metastatic deposits have been described in the liver, the kidneys, and the ovaries, but it is probable that these tumors belong in the group of sarcomata rather than to the gliomata.

Neuroglioma ganglionare is a growth composed of neuroglia, of ganglion-cells, and of nerve-fibres, and it may be diffused or be circumscribed. A portion of the tumor undergoes a myxomatous change occasionally, and these growths are then known as *myxoglioma*. In other cases there may be a combination with sarcoma (gliosarcoma). Glioma is rarely found in the cerebellum. When extensive degenerative changes occur in glioma it is often difficult to recognize the new formation, which is not suited to surgical interference, owing to its ill-defined outline.

The subject of *syringomyelia*, that has been so much discussed of late in neurological literature, deserves consideration in connection with the general subject of glioma. The prevalent view is that in such cases, owing to a lack of developmental differentiation, there is a growth of quasi-embryonic tissue of the spinal cord specially involving the neighborhood of the posterior commissure and the posterior gray horns. Sometimes, also, there is an imperfect closure of the posterior cleft. Eventually, this gliomatous tissue is liable to break down, giving rise to the formation of cavities which are generally lined with pieces of membrane. This condition is commonly met with in the cervical portion of the cord, but occasionally in other parts as well. It is sometimes associated with spina bifida and sometimes with hydrocephalus.

The clinical symptoms which are most characteristic are a loss of the sense of pain and of temperature in certain well-defined areas, associated with a relative preservation of the sense of touch. There is also a high degree of muscular atrophy, which usually occupies a smaller area than the sensory disorders. The disease is progressive and is not amenable to surgical treatment.

9. Chondroma.

Enchondroma, or chondroma, is a tumor which consists of cartilage. It occurs principally where cartilage is found normally—that is, on the bones and in the cartilage of the respiratory organs—but it may also be found where there is no cartilage.

Virchow divided the chondromata into two forms: those which grow from cartilage, or the ecchondromata, and those which grow independently of cartilage, or the enchondromata. The former class is, however, a small one, the great majority of cartilaginous tumors belonging to the class of enchondromata.

Enchondroma varies greatly in size. It may appear as a small round tumor or as a large lobulated growth (Fig. 120). It consists of either hyaline cartilage or of fibro-cartilage. The tumor may be in a state of mucous softening or be partially ossified. It may also be composed of osteoid tissue, such as is found in the ossifying callus between the bone and the periosteum, and it is then known as *osteoid chondroma* (Virchow).

The tumor consists not only of cartilage, but also of connective tissue, which, however, is usually small in quantity. It separates

Fig. 120.—Enchondroma of the Tibia, just below knee-joint (female; duration five years).

the cartilage into numerous lobules. At times the fibrous tissue may preponderate to such an extent that very little cartilage is seen. The cells vary greatly in size, in form, and in numbers in different tumors and even in the same tumor. At times they are so numerous as to crowd against one another and leave little intercellular substance. They may be exceedingly few in number in other growths. They are often quite large, and contain one or more nuclei and a well-marked capsule. In other cases the capsule is wanting (Fig. 121). In some forms the cells are stellate with anastomosing prolongations: in these tumors the tissue is usually soft, and it has the åppearance of myxoma. The intercellular

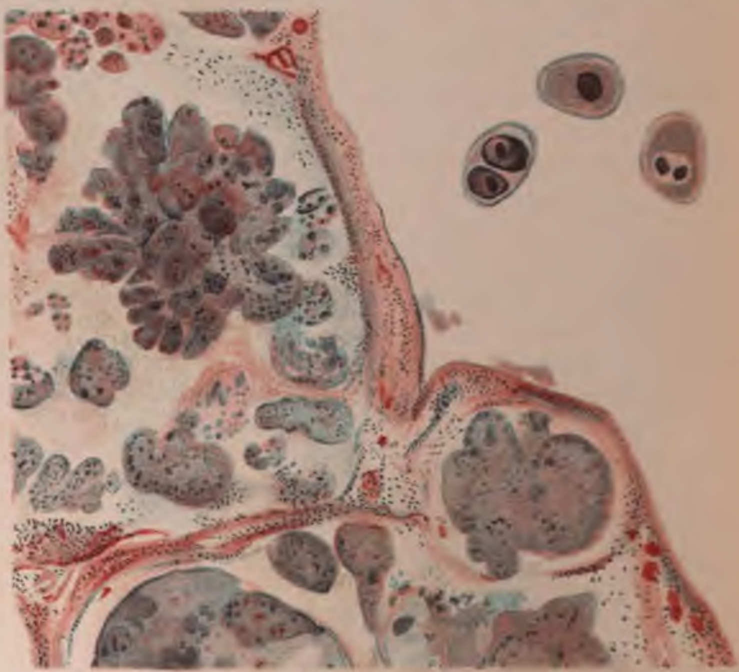

FIG. 121.—Hyaline Enchondroma (oc. 3, obj. D., and oc. 3, obj. A.; hematoxylin staining).

substance is either hyaline or fibrous. Chondroma may be combined with sarcoma.

Cartilaginous tumors may undergo a mucous softening so far as the intercellular substance is concerned, and the cells in this case undergo fatty degeneration: these changes lead to the formation of cysts. These tumors may also undergo calcification or ossification. At times chondroma may be highly vascular. Chondroma occurs most frequently during youth, at a time when the bones are developing: there is probably some connection between the formation of these tumors and irregularities in the development of bones. According to Birch-Hirschfeld, trauma appears to exert a decided influence upon the origin of this form of tumor. Enchondroma is often found on the long bones, and particularly upon the phalanges of the hand or upon the metatarsal bones (Fig. 122). It is observed on the larger long bones, on the scapula, on the bones of the cranium, on the jaws, and on the ribs. It is found also in the testicle, the parotid gland, the mammary and submaxillary glands, and the lungs.


FIG. 122.—Enchondroma of the Thumb.

Virchow has given the name of *ecchondrosis* to those cartilaginous tumors that grow directly from cartilage. Small cartilaginous tumors are found in the thyroid cartilage and in the rings of the trachea, and also in the epiphyseal lines and in articular cartilage. They are found also on the costal cartilages, on the synchondroses, and on the intervertebral cartilages. Those that grow from the articular cartilage are often separated from their

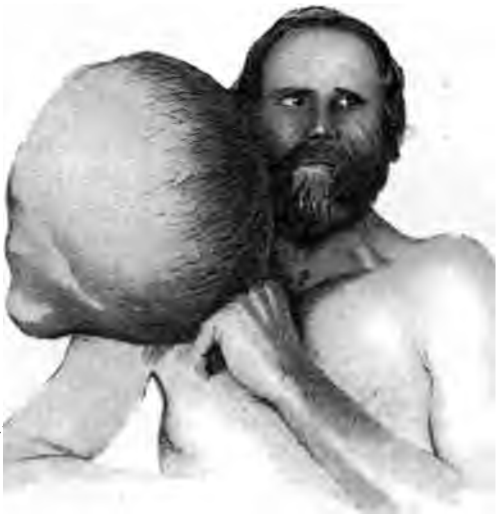
FIG. 123.—Mixed Cartilaginous Tumor of the Parotid Gland.

base and wander about within the joint. These tumors are known as "loose cartilages" or "joint mice." They may spring also from the synovial membrane or from the periosteum. They give rise to considerable irritation and effusion in the joint, but they may eventually become anchored in some pouch of the articular capsule. If a spontaneous cure does not occur in this way and they continue to give trouble, they should be excised.

One of the most frequent of the fibro-cartilaginous tumors is the "mixed cartilaginous" tumor of Paget, which grows in the interstitial tissues of the parotid gland. In these tumors are seen numerous cylindrical masses of epithelial cells which are of glandular origin. These tumors are of slow growth and are nodular, and they can easily be separated from the tissue of the parotid gland. If allowed to grow, they may eventually attain an enormous size (Fig. 123).

The *hyaline enchondroma* is also of slow growth, but it may at times assume immense proportions, as shown in the scapula of the patient whose portrait is here given (Fig. 124).


FIG. 124.—Hyaline Enchondroma of the Scapula.

The *osteoid chondroma* has a fibrous appearance. It develops from the periosteum, and it may form a spindle-shaped growth of considerable size in the long bones. These tumors are often sarcomatous, and Billroth prefers to classify them with the periosteal sarcomata.

Chondroma is a benign growth, but in the rapidly-growing forms the cell-growth is abundant, and the transition from chondroma to sarcoma not infrequently occurs in portions of the tumor.

Metastatic deposits of chondroma are to be distinguished from multiple chondromata, which are occasionally seen. Schuh reports the case of a girl, twelve years of age, who had such tumors on all the bones except those of the head and the spine. Chondromata show a tendency to break into the blood-vessels and the lymphatics, and portions of the growth are transmitted by embolism to distant organs, particularly the lungs.

10. Osteoma.

Osteoma signifies a tumor composed of bony tissue. There are, however, several forms of bony growth which should not be regarded as tumors. Such are the osteophytes, which form as the result of an inflammation of the periosteum; the diffuse enlargements of bones, such as have already been studied; and the ossification of tendons and muscles. An osteoma may grow upon the surface of the bone, and it is then called an "exostosis;" or it may grow in the interior of the bone as a firm bony nodule, and it is called an "enostosis." It may also grow quite independently of bone, and it is this variety which Virchow regards as heterologous.

Osteomata are placed in two different classes, according to the character of the bony substance of which they are composed. There are the hard or eburnated osteoma and the spongy osteoma.

Fig. 125.—Ivory Exostosis of the Orbit.

The most characteristic variety of *osteoma durum* is the *ivory exostosis* which occurs in the bones of the skull and the face (Fig. 125). It consists of a thick osseous tissue which is arranged in the form of concentric parallel lamellæ: in the lamellæ the bone-corpuscles are so arranged that their prolongations are directed toward the periphery of the tumor. The vessels are exceedingly few in number. The surface of the tumor is nodular and is covered by a thin layer of periosteum. There are also dense forms of osteoma that resemble more closely the structure of cortical bone.

The ivory exostosis is found most frequently in the frontal bone, and it encroaches upon both the cavities of the cranium and the orbit, compressing the brain and protruding over both eyes (Paget). These tumors grow in the diploë or sinuses as isolated or as narrowly-attached masses. The size and situation of these growths make their removal often impossible, although in the simpler kinds operations have been performed with success. Their slight attachment is not infrequently destroyed, and necrosis follows and the tumors may be discharged spontaneously. Hutchinson describes such a growth lying loose in the orbit, which growth after its removal left a cavity nearly the size of the fist, over the upper and inner cavities of which the brain could be felt pulsating. The Warren Museum possesses the frontal bone of a patient from whom a portion of such a tumor was removed. The *odontoma* also consists of a dense ivory structure, and it may spring from the tooth or from the alveolar process. It is often associated with an irregularly-developed tooth. Hard osseous tumors have also been found on the lower jaw (Fig. 126).

FIG. 126.—Osteoma of the Lower Jaw.

Osteoma spongiosum contains in its interior more or less well-marked medullary tissue and spongy bone. These tumors are found growing from the epiphyseal lines of long bones, and are usually covered with a thin layer of cartilage. They are attached to the bone by a more or less well-defined pedicle. Sometimes they are partially covered by a bursa filled with fluid, which gives them the appearance of being much larger than they really are. The writer has removed such tumors also from the scapula, and they may be found on other flat bones. Another form of spongy osteoma is the so-called "subungual exostosis," which, according to Birch-Hirschfeld, is a periosteal growth. It is found not infrequently growing beneath the nail of the great toe. This growth also has frequently a cartilaginous surface.

All these spongy osteomata grow to a certain size and then cease growing. With the exception of the last named they give little trouble. Occasionally, however, they reach an unusual size, and cases are reported in which the tumor grew to be as large as a man's head.

Osteoma of bone develops either from the connective tissue of the periosteum or from cartilage or from the medullary tissue. Osteoma is also found entirely independent of bone. Such growths have been observed in the brain: they are supposed to develop from the neuroglia, and they have been regarded as an ossifying encephalitis (Birch-Hirschfeld). They also spring from the meninges. Bony tumors are found in the eye and in the lungs, and miliary bony tumors are also seen, though rarely, in the skin. Multiple osteomata are seen not only upon the bones of the skull and other flat bones, but also upon the long bones.

In regard to the etiology of osteoma, it is supposed by many that there is an hereditary predisposition, particularly in cases of multiple osteoma. These tumors appear occasionally after injuries. Syphilis and gout are also supposed at times to exert an influence favorable to the development of bony growths. The prognosis of osteoma is favorable, as it is strictly a benign tumor.

11. NEUROMA.

"Neuroma" is a term originally applied to a tumor supposed to consist of nerve-tissue. Many of these tumors prove on microscopical examination to be composed of nerve-tissue to a limited extent only, the bulk of the growth consisting of fibrous tissue. A new formation of nerve-tissue does, however, occur. The term *neuroma fibrillare* is used to indicate growths of nerve-fibres. Neuroma cellulare is a tumor consisting of new-formed ganglion-cells. When the tumor is composed of fibres which contain no myelin, it is spoken of as a "neuroma amyelinicum." When the fibres contain myelin, the growth is called "neuroma myelenicum."

Neuroma cellulare is an exceedingly rare growth. One case is reported as existing in the ala of the nose of a man thirty-one years of age. It is more frequently found in the brain, usually in the lateral ventricle. A growth of ganglion-cells may be found in a teratoma of the ovary or the testicle, and also in congenital sacral tumors.

Neuroma myelinicum occurs either as a circumscribed round or lobulated nodule, as a spindle-shaped tumor, or as a diffuse thickening of a nerve arranged in knots or in loops. It consists of a mass of firm, grayish-white tissue, composed of interlacing bundles of fibres, between which is a moderate amount of loose connective tissue poorly supplied with blood-vessels. A microscopic examination shows the myelin-fibres, which are stained black by hyperosmic acid.

The *amyelinic neuroma* is a yellowish or a whitish-gray tumor of considerable firmness, having somewhat the appearance on section of a fibroma. Under the microscope the nerve-fibres with their nuclei can be made out by picking them gently apart (Winiwarter).

Neuroma may occur either singly or as a multiple tumor, and it is accompanied by an increase in the connective tissue of the nerve, particularly of the outer (and less frequently of the inner) layers of the endoneurium, so that the bundles of nerve-fibres at the seat of the tumor are surrounded by a loose growth of connective tissue. The perineurium may also be involved in this growth, but the epineurium is rarely affected. Such a tumor is therefore, strictly speaking, a neurofibroma.

Multiple neuromata may be found existing at several points in a nerve-trunk, or they may be situated in the various branches of a nerve, or they may be indiscriminately distributed throughout the body. A single neuroma is more likely to be painful than the multiple form. The nervous disturbance depends, however, upon the attachment of the tumor to the nerve. If it is so situated that the nerve-fibres are compressed, whether the tumor be central or be peripheral there is more likely to be pain than when the fibres are spread out tape-like over the tumor. Multiple neuromata may be seen as a string of nodules following the course of a nerve-trunk, or as nodular growths spread out beneath the skin in various directions. They are usually movable. If adherent to the surrounding structures, there is a possibility that the growth may be sarcomatous—a combination that not infrequently occurs.

Many neuromata are congenital or they appear during the early years of life. They are not infrequently found in persons of defective mental development. Heredity appears to exert an important influence, as multiple neuroma is often seen in various members of a family. Acquired neuromata appear between the ages of twenty and forty years.

The so-called "*malignant neuroma*" is usually neurosarcoma or neuromyxoma. There is in these growths a new formation of nerve-fibre, but their principal feature is the malignant element, and these tumors may be the origin of metastatic deposits. The neuroma amyelinicum may suddenly change its benign nature and become converted into a malignant growth.

Plexiform neuroma consists of a convolution of numerous bundles of fibres which have nodular swellings at various points, and which are intertwined in a tangled mass. They are held together by a loose connective tissue that lies in a fold of skin, which is hypertrophied and pigmented and covered with a thick, coarse hair. The tumor is congenital, and it is usually situated on the scalp, on the neck, or on the cheek. There is a thickening also of the connective-tissue structures of the skin, particularly those surrounding the vessels and the hair-follicles, such as has already been described in the case of multiple fibromata. The growth is regarded by many as a local congenital elephantiasis of the nerves. The neuroma found in the ends of divided nerves is the form of tumor with which the surgeon is most familiar. Such growths occur both in the peripheral and in the central end of a nerve which has been divided in continuity, and are often observed by the surgeon who lays bare the nerve for the purpose of uniting the severed ends. But the commonest form is that found in amputation-stumps, and it is the cause often of intense neuralgic pain (Fig. 127). It is evident that these growths are the result of an abortive attempt at repair of the injured nerve, and there is found here virtually the same process going on which has already been described in the section devoted to the repair of nerve-fibres. There is a growth of the nerve-cylinders, which are imbedded in a mass of fibrous tissue forming around the end of the nerve. Such tumors appear to form in the nerves of the stump of an amputated arm more frequently than elsewhere.

FIG. 127.—Neuroma from an Amputation-stump (Sp. 1154, Warren Museum).

The excision of a portion of the affected nerve-trunk usually results in a cure of the neuralgia. Occasionally the pain returns. Winiwarter invented an ingenious operation to meet the difficulties presenting in an obstinate case. On one occasion he divided the brachial plexus above the clavicle and united the central stumps of the nerves in pairs, so that the peripheral portion should completely be isolated. This operation was successful.

A form of tumor which is generally supposed to be a neuroma is the so-called "*painful subcutaneous tumor*" described by Paget. It is usually found in the extremities, especially the lower. Very rarely it occurs on the trunk and the face. It is seen more frequently in women than in men. It consists of a small tumor situated just beneath the skin. Occasionally amyelinic nerve-fibres are found in it, but it may consist also of a loose or a dense connective tissue or of fibro-cartilage. Some of these little tumors proved to be leiomyoma and others angioma, and still others adenoma of the sweat-glands. Their structure is therefore not characteristic of any particular variety of tumor, and the pain is probably due to the involvement of some sensitive nerve-fibre in the growth.

12. MYOMA.

Tumors composed of muscular fibre are divided into two classes. To the first class belongs the *leiomyma*, or a tumor made up of unstriped muscular fibre; to the second belongs *rhabdomyoma*, a much rarer form, which is composed of cells closely resembling striped muscular fibre. Virchow named these two forms "myoma lævicellulare" and "myoma striocellulare," respectively.

Leiomyoma is found most frequently in the uterus, and occasionally also in the muscular layer of the intestine and the urinary organs. It is also seen, though rarely, in the ovary; it is likewise found in rare instances in the skin and in the subcutaneous cellular tissue. The muscular cells are arranged in bundles which run in straight or in wavy masses more or less parallel with one another. Many bundles, however, are found running at right angles or more or less obliquely to the others. Between these bundles there exists a more or less vascular connective tissue. When properly stained the long staff-shaped nuclei are brought out quite distinctly, and the cells are then seen to exist in great numbers (Fig. 128). The

FIG. 128.—Myoma of the Uterus.

cells may be isolated by picking them apart in the fresh state, by allowing them to remain for twenty-four hours in a 20 per cent. solution of nitric acid, or by placing them for twenty or thirty minutes in potash. In the small and succulent myomata of the uterus the tissue is made up almost entirely of muscular fibre. In the large tumors a considerable portion of the substance of the growth consists of a firm, dense fibrous tissue. These tumors are called "fibromyomata." In some cases the connective-tissue growth is soft and areolar, and such tumors are much less dense. Myoma is not usually a vascular tumor, but in some cases the development of blood-vessels is quite marked. In other specimens larger lymph-spaces are found between the bundles of fibres, and at times there are seen cysts of considerable size, due to a dilatation of these spaces. Nerves are occasionally also seen in these growths. The fibrous portions of these tumors appear as a glistening white, almost tendinous, tissue; the muscular portion, as a reddish-white or a gray structure.

The growth of these tumors in the uterus is exceedingly slow, but they may eventually assume a greater size than that of any other known tumor. They may be single or multiple. They may grow on the outer wall of the uterus, and in that case they project into the peritoneal cavity. Such tumors are known as *subserous myomata*. When the growth originates in the middle layers of the uterine wall the tumor is called an "interstitial myoma." Those growths projecting into the cavity of the uterus are known as "submucous myomata." All these forms may occur in the cervix as well as in the body of the uterus.

Uterine myoma frequently undergoes considerable changes in volume, increasing materially in size at the period of menstruation. Many of the changes are produced by the increased flow of blood or by a dilatation of the lymph-spaces. A marked decrease in its size may be produced by contraction of the muscular fibre, particularly when it is subjected to the long-continued action of ergot. Uterine myomata may undergo softening. This change occurs in large growths, and it is due to disturbance of circulation. Fatty degeneration and cysts are seen under such conditions. Calcification occurs in old myomata, particularly in those attached by a narrow pedicle. The change takes place in the connective tissue, the muscular fibres undergoing at the same time fatty degeneration. In some cases osteoid tissue is found, and some of these tumors have a bone-like hardness.

Many cases of leiomyoma have been reported growing in the stomach and in the intestinal canal. It is only in exceedingly rare instances that they attain a large size. The growth is found in the ovary, and it may produce a large solid ovarian tumor. Such a tumor was recently removed by the writer from a woman about forty-five years of age, and it had a large amount of unstriped muscular fibre. It was about the size of a child's head and weighed eight and a half pounds.

Many of the cases of enlarged prostate are due to a new formation of muscular fibre. In some cases there is general hypertrophy of all the constituent parts of the gland; in other cases the glandular structures appear to form the greater part of the growth. The principal seat of the muscular growth is in the upper and posterior portions of the gland in the condition known as hypertrophy of the middle lobe (Birch-Hirschfeld).

Myoma of the skin is always composed of unstriped muscular fibres. The development of the new muscular cells takes place either from the muscular walls of the blood-vessels, from the erectores pilorum, or from those muscular structures seen in the subcutaneous tissue in the scrotum, the labia, the nipples, or the face.

Pure myoma of the skin or of the subcutaneous tissue may either be solitary or be multiple, and it usually grows to the size of a cherry. It is moderately soft, and it appears on section as a reddish-white tissue resembling either a sarcoma or a fibroma according to its density. It may be found in the scrotum, the labia, or the nipple, or in almost any region of the body. When situated in the skin it appears as a yellowish-red or a dark-red tumor. It is found more frequently in young people, and is probably in most cases congenital. Many of the cases of true keloid are undoubtedly partly muscular in structure; hence they should be regarded as fibromyomata. Combinations of myoma with sarcoma rarely occur. In angioma the walls of the blood-vessels or the vascular spaces are composed of muscular fibre, which frequently constitutes the principal portion of the tumor. Such a tumor should, therefore, be called "angiomyoma." Diffuse forms of myoma are seen in those cases of hypertrophy of the skin of the scrotum partaking of the character of elephantiasis.

Rhabdomyoma, or a tumor consisting of striped muscular fibre, is a rare growth as an independent tumor. It is found more frequently in combination with sarcoma. Bands of spindle-cells with striæ are then seen. A pure rhabdomyoma contains bands of these cells that are marked more or less clearly with striations. In addition to long spindle-shaped fibres there are seen round or club-shaped cells with or without prolongations (Ziegler). Rhabdomyoma is found in the testicle, in the heart, and in the muscular system. Myosarcoma is found in the kidney and in the testicle. It has been observed also in the stroma of an ovarian cyst and in certain forms of teratoma.

13. Angioma.

The name *angioma* is given to tumors the main portion of which is composed of new-formed blood-vessels. There are two principal varieties of angioma—the plexiform angioma or nævus and the cavernous angioma. In the former there is presented a tumor composed of vessels which have preserved their character. In the latter there are no distinct vessels, but there is a spongy tissue composed of a stroma containing spaces lined with endothelium and resembling the erectile tissue.

Plexiform angioma, teleangiectasis, or nævus is of two kinds. The superficial forms of nævus, or "mother's marks," appear either as bright-red or claret-colored marks upon the skin or as slightly raised portions of the skin also stained a deep red. In the former the skin appears to be unaltered as to texture. These discolorations appear to be due to an enlargement of the capillary vessels in the papillæ from which spring other vessels. The outline of these spots is either well defined or there are a number of minute prolongations running in varying directions. Minute blemishes of this kind, which are not uncommon on the nose or the cheeks of young children, are popularly known as "spider cancers" (nævus aranæus), and the larger spots are known as "port-wine marks."

Occasionally the skin appears to be hypertrophied and coarse-grained, which is due to hypertrophy of the papillæ. These spots appear at or soon after birth, and they may increase considerably in size, but usually they do not materially change. In the cavernous form the vascular structure is more developed. Here one finds coils of capillary vessels or arterioles which are grouped together in lobules, and which have apparently taken their origin in the subcutaneous adipose tissue, and gradually worked their way up through the channels of the skin to the surface, where they make their appearance soon after birth. They are raised somewhat above the surface of the skin, and have a bright-red color, with a slightly irregular border. The part beneath the skin is much more extensive than that which appears upon the surface. When pressed upon firmly the vessels are emptied of their blood and the tumor disappears, but it is soon again filled by faintly-pulsating waves.

In some of these growths the muscular cells are very numerous, and the vessels are then usually narrow. These growths are known as "angiomyomata." Sometimes the walls of the vessels are very thin, and they here and there present varicosities. Such conditions are found in angioma of the brain and in a teleangiectatic condition of certain tumors. Plexiform angiomata, or nævi, are found principally upon the head, the neck, and the chest. They are rarely found on the mucous membrane or on the serous surfaces of the liver, the spleen, or the kidney. They are often multiple.

The more vascular forms of nævus sometimes become very formidable growths, and they are difficult to arrest in their progress, covering as they do large surfaces and ultimately causing death from hemorrhage (Fig. 129). Fortunately, this class is rare, and the little tumors if excised do not return. The smallest nævi may be cured by puncture with a hot needle or with the fine point of a Paquelin cautery. The port-wine marks, which are usually too extensive for excision, are not affected by any other treatment. They do not, however, tend to grow beyond a certain point. The cavernous angioma is composed of tissue like that of the corpora cavernosa.

FIG. 129.—Angioma of the Lip and the Neck.

It is probable that the pure form of this disease develops from the venous capillaries by a process of budding of solid masses of protoplasm, which subsequently became hollowed out and converted into cavernous tissue. It is supposed that in some cases the growth develops from the capillaries of the part, which become dilated and fused together. In other cases it is possible that communication takes place between previously-formed spaces (lymph-spaces) and the veins. The stroma consists of a connective-tissue trabeculæ, which surround spaces whose walls are lined with endothelium, and in which spaces the blood is largely venous (Fig. 130). It is only in rare cases that these tumors communicate with a large arterial branch. Nerves are sometimes found in these tumors, and the muscular cells are often seen in large numbers.

The tumor appears as a raised and lobulated mass occupying the skin or the subcutaneous tissue, with a more or less well-defined outline. The color is either that of the skin or of a deep-blue shade. When connected with the arterial system the color is a bright red.

Nævi are found not only on the surface of the body, but more rarely also in the muscles, the glands, and the bones. Their com-

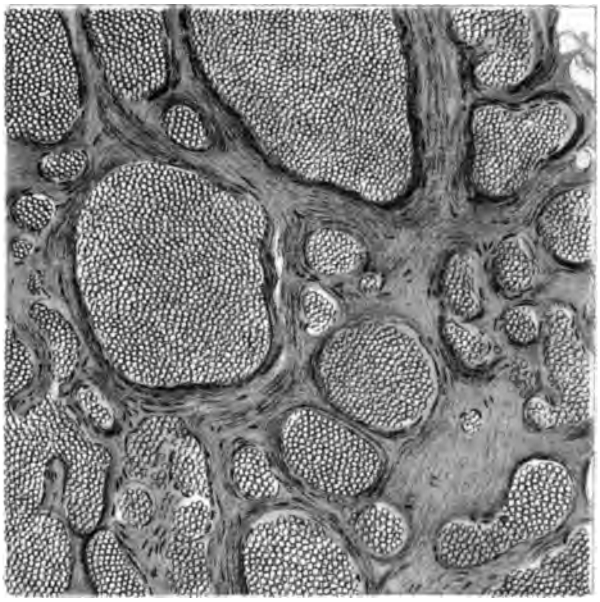

FIG. 130.—Cavernous Angioma.

monest seat in the internal organs is the liver, but they are seen also in some instances in the uterus, in the intestine, and in the bladder.

The cavernous angioma is rarely congenital, but it appears rather late in life in the internal organs, and during the first half of life it appears in the skin and the subcutaneous tissue. Many of these tumors are exquisitely sensitive. They grow slowly, but they may become quite formidable and dangerous, owing to their size and to their liability to hemorrhage.

The accompanying drawing shows such a growth upon the scalp of a young man (Fig. 131). It was removed by an almost bloodless operation with the Paquelin knife. There were in the neighborhood several smaller wart-like angiomata, which, as they had not increased in size, were not treated. In cases where the growth is too deep for excision the cautery may be used or a deep ligature may be made to encircle the mass.

FIG. 131.—Angioma of the Scalp.

Angioma venosum, or *varix*, is a tumor composed of dilated veins, such as are seen in hemorrhoidal tumors. They are found also in the face and the neck and in the scrotum and the labia. Some of these tumors are simply dilated veins; others are probably formed by a new development of venous blood-vessels, particularly those in the face and the neck.

Aneurisma racemosum, or *cirsoid aneurism*, resembles the varix closely, but it is composed of dilated arteries instead of veins (varix arterialis). This dilatation is found in arteries of medium size, and principally upon the head, on the upper extremity, and on the back. Most of these tumors are composed of arteries of new formation, and are therefore genuine tumors. The growth of new arteries occurs very much in the same way that new vessels form in the healing of wounds. These growths are sometimes most formidable affairs.

Such a case occurred in the hospital service of the late Dr. G. H. Gay. The tumor, which covered the median portion of the scalp, had a prolongation that divided on the bridge of the nose and ran obliquely across each cheek. Near the vertex the mass appeared to consist of one or two large chambers, and radiating from the main body of the tumor were large arteries occupying the seat of the temporal, occipital, and facial vessels. The writer was called to the hospital to see the patient, and he found him with an abdominal tourniquet applied to a rupture on the top of the tumor. On removing this compress a perfect geyser of blood spurted up to the height of a foot into the air. This discharge emptied the sac, which was seized and ligatured. The writer ligatured several of the large arteries. A few weeks later Dr. Gay transfixed the growth with long needles and over them passed figure-of-8 ligatures. The mass sloughed away and left a healthy granulating surface which healed. About fifteen years later the writer removed an epithelioma from the nose of this patient, on whom there was hardly a trace of the old scar.

A tumor of precisely the same description is given in Ziegler's

Pathological Anatomy. In the case reported the vessels seem to have fused together, forming in the tumor several large chambers.

14. LYMPHANGIOMA.

Lymphangioma is a tumor which bears the same relation to the lymphatics that angioma does to the blood-vessels. It consists of a connective-tissue network the meshes of which contain lymph-spaces lined with an endothelium. In addition to the connective-tissue stroma there exists often fibrous tissue and adipose tissue, and occasionally numerous blood-vessels. The following described three varieties are recognized: The lymphangioma simplex, or teleangiectasia lymphatica, which consists of a congeries of dilated lymphatic vessels that are in part a new formation and in part a dilatation of pre-existing vessels: according to Wegner, this variety is due to an obstruction in the lymphatic circulation, and it is analogous to the venous varix; the lymphangioma cavernosum, which consists of a stroma that surrounds cavities formed by the fusion of pre-existing and new-formed lymphatic vessels and of lymph-spaces filled with lymph (Winiwarter); the lymphangioma cystoides, which consists of a cyst, simple or compound, filled with lymph, supposed to be formed by the fusion of the lymph-spaces of a cavernous lymphangioma.

Lymphangioma is a rare form of tumor. It is frequently congenital, but it may also be an acquired growth. It is found in the skin and the subcutaneous tissue, and also in the tongue, the gums, and the lips, as well as in the scrotum and the labium. The writer has seen a well-marked cavernous angioma in the skin of the back of an adult and in the axilla of a child.

The simple lymphangioma is often accompanied by an œdema and thickening of the skin, which condition has been called "elephantiasis" or "pachydermia lymphangiectatica." Such conditions are found in the scrotum, the penis, the prepuce, the clitoris, the labia majora, etc. It is found also in the tongue in macroglossia, and on the conjunctiva. It often forms a part of the congenital diffuse hypertrophies of the lips and the cheeks. According to Virchow, in tropical countries lymphangiectasia may occur in bunches of lymph-glands. This form of lymphangioma may be circumscribed or be diffuse. Occasionally perforation may take place at some point, and a lymph-fistula is developed from which a clear serum exudes drop by drop.

The *cavernous lymphangioma* consists of a number of large lymph-spaces communicating more or less perfectly with one another and containing a clear or a milky fluid. It appears as a soft, more or less fluctuating tumor on the face, the trunk, or the extremities, and it is easily mistaken for a lipoma or an angioma, and even after operation it is often difficult to decide as to the exact nature of the growth. The accompanying drawing is a portrait of the cavernous type (Fig. 132). One of the lobes was aspirated and the child died of septicæmia.


FIG. 132.—Lymphangioma.

Cystic lymphangioma, which is usually found in the neck, is one form of hydrocele of the neck. It should, however, be remembered that a certain number of these cases of hydrocele are branchial cysts, as has already been seen. The cyst is lined with endothelium, and it may contain either a clear or a bloody fluid. Some of these cysts run in between the muscles. Winiwarter reports such a complicated cyst associated with macroglossia.

These cysts are situated in the upper part of the neck, and they may send prolongations as far as the mediastinum. In one case which came under the writer's care there was a swelling beneath the angle of the jaw, on opening which swelling a large quantity of clear serum escaped. The ramifications of the cyst were so extensive that it was impossible to follow them. The patient was an adult. Most of these cases of hydrocele, however, are congenital, but they grow slowly. Congenital cystic lymphangioma is also found between the skin and the sacrum.

The operative treatment of these tumors at the present time is not nearly so dangerous a proceeding as formerly, but the direct communication with the lymphatic system renders such cases liable to general septic infection if strict asepsis is not observed. In the cases of hypertrophy wedge-shaped masses should be excised to relieve the deformity. Many of the well-defined forms of lymphangioma can be extirpated: when this is not possible free incision should be made, and the cavities should be stuffed with an aseptic or iodoform gauze.

15. Psammoma.

Psammoma is a growth usually found on the membranes of the brain, and it contains calcareous concretions. Particles of sand are found in the pineal gland, on the choroid plexus, in the Pacchionian bodies, and in small bodies on the dura mater. Tumors containing sand are found occasionally also in the lymphatic glands, the thymus gland, and on the capsule of the testicle. They may also be found in sarcomatous and in carcinomatous growths.

The particles of sand are scattered over the tumor, and they are found lying either in a connective-tissue stroma which has undergone a hyaline degeneration, or are surrounded by concentric layers of cells, which, according to many observers, are endothelial in character. The origin of these concretions, according to Birch-Hirschfeld and others, is due to a retrograde change in a growth of bud-like sprouts from the walls of the blood-vessels. The only specimen examined by the writer was a tumor the size of a pigeon's egg which was removed from the dura mater. It was white and had a fibrous appearance. Microscopically, it consisted of numerous concretions surrounded by cells apparently of an endothelial nature. There were numerous fibrous septa which supported this rich cell-structure. The fibrous forms of psammoma are benign growths, but it is well to remember that these concretions may also be found in malignant tumors.

XXXII. ASEPTIC AND ANTISEPTIC SURGERY.

THE student who walks the surgical wards of a hospital to-day, and sees about him the comfortable patients with their artistic surgical dressings, has little or no conception of the dangers that beset a convalescent from a surgical operation before the antiseptic era, and it would be a difficult task to paint to him in their true light the horrors of a great metropolitan hospital in olden times. An old French writer gives this glimpse of the Hôtel Dieu in 1515, while it was still a comparatively small hospital, containing but three hundred and three beds: "En chacun desquels par faute d'aisance on voit ordinairement huit dix et douze pauvres en ung lict, si très pressés que c'est grand pitié de les voirs" (Husson).

In 1740, a year in which there was a very severe and long winter, the Hôtel Dieu received 26,705 patients and the number of deaths was 7894. The larger beds contained from four to six persons. Reports written by Tenon and a committee of the Academy just previous to the Revolution show most clearly to what depths of misery the common people must have fallen to accept the shelter of this hospital.

In the surgical ward there were, on January 6, 1776, 273 patients, there being but 106 beds in the ward. The walls were soiled with expectorations and the floors with evacuations of the bowels and bladders, as also with blood and discharges from the wounds. The wood-supply and the washing were kept in this ward, and every afternoon there was also an out-patient clinic. There were four rows of beds in a ward thirty-four feet wide, and the report states: "It is difficult to maintain the purity of the air on account of the blood and pus that stain the floor, which it is impossible to clean, owing to the crowding of the beds."

In the St. Jerome Ward more operations were performed than in any other ward in Europe. It was placed almost directly over the dead-house, the odors of which were quite perceptible. This ward accommodated about 20 beds and an out-patient department. The capacity of the hospital was 2500 beds, but during the cold season as many as 4800 patients were in the hospital at one time.

On the straw beds there were sometimes four or five patients called "agonisans." These patients were not only the moribund, but also those whose sphincters were beyond control. These beds were only occasionally wiped with a cloth, and the straw was rarely changed. On extraordinary occasions the patients were placed in tiers one above another, so that some were reached only by a ladder. There were no stoves, the wards being warmed only by the presence of the patients.

The mortality before the Revolution was one death to every 4.5 patients who entered the hospital; and this mortality of course included many who were hardly ill, the insane, and the pregnant women. Unfortunately, the writer has been unable to obtain statistics of certain operations, which were evidently concealed from those attempting to investigate. The only statement discovered was that in 1740 the operation for trephining was always fatal, but one can easily imagine the state of wounds under such unfavorable conditions.

In more humane communities surgery was less resorted to, and the records of the Massachusetts General Hospital show that the number of surgical operations in the early part of the present century was incredibly small as compared with those of to-day. At the time of the introduction of ether (1846) the cases that Dr. Warren had at his disposal on which to try this anæsthetic were few and far between. The advent of anæsthesia brought with it apparently a great increase everywhere in the number of operations performed, but it did not diminish the dangers of convalescence. In the period immediately preceding the discoveries of Lister epidemics of gangrene and of erysipelas were rife, and no capital operation could be performed without grave doubts as to the future of the patient.

It is not improbable that the ancients had some idea of the antiseptic treatment of wounds. According to Dr. Anagnostakis, professor in the University at Athens, the Greek physicians were acquainted not merely with σηψίς (putrefaction) and ἄσηπτος (non-putrescible), but they also recognized the fact that decomposition of the blood was the most important factor in the prevention of the healing of wounds, and that it was the cause of suppuration. Hippocrates was aware that moisture favored putrefaction, and he urged strongly that wounds should be kept dry. The antiseptic properties of alcohol and tar were likewise known, as well as the use of aromatics and resins and the great advantage of clean dressings.

When Lister first introduced his method of treating wounds, based upon Pasteur's theories in regard to the action of bacteria in producing fermentation, the air was supposed by him to be the medium through which organisms were conveyed to the wound. Previous to that time the air had been supposed to exert an unfavorable action upon freshly-wounded surfaces, and to the *action of the air* was ascribed the suppuration which occurred in compound fractures. Tyndall's investigations upon the dust of the air seemed to confirm this view. It is now known that the organisms found in the air consist of the spores of mould or yeast-fungi, as well as of bacteria. While the bacteria are more numerous in the air of a room, the fungi predominate in the open air. The number of micro-organisms varies greatly, according to the locality and to the moisture of the atmosphere. The air of cities contains more organisms than that of the country. After a heavy rain or a fall of snow the air is almost completely free from germs, and this condition is habitual on the ocean and in the regions of perpetual snow. The conditions that favor the growth of bacteria are not found in the air. The necessary warmth, moisture, and nutritive material do not exist in the air. In fact, conditions exist which are extremely unfavorable to certain organisms, such as the anaërobic bacteria. Dryness and sunlight are also unfavorable to the life of all bacteria. One should not, therefore, expect to find pathogenic organisms in the air, but in organic substances. Here they find a soil suitable for their growth, and it is only when the warm and moist soil is converted into dry dust that these organisms are temporarily blown about in the air. The bacteria swarming in foul water are, therefore, not conveyed to the atmosphere, and thus it happens that the foul air emanating from moist and putrefying substances, such as exists in canals or in privies, contains fewer bacteria than the air of the street or the garden. It is for this reason that a celebrated surgeon exclaimed: "I would be willing to operate in a water-closet if my hands were only clean.".

It has been found by careful observations that the air of operating-theatres is usually most impure in the morning after the room has been "dusted," and that it gradually increases in purity during the day. In the same room, immediately after a lecture, there is a marked increase in the quantity of bacteria. This increase is due to the disturbance of the dust which had settled down, and not to the poisonous nature of the expired air of the large number of individuals present. The foul air thus produced is due to the presence of gases, and not to bacteria. Tyndall demonstrated that expired air is free from germs, and Straus showed that the bacteria in the air of a lecture-room full of pupils actually diminish in numbers during the lecture-hour, the air-passages acting as filters to the micro-organisms. The infection of a wound from the breath of a surgeon is, according to Schimmelbusch, not to be feared, and the breath of a septic patient cannot contaminate the atmosphere of a ward.

The danger of infection from the air is, therefore, slight as compared with a direct contact with infectious material. A cubic metre of air may contain from 1000 to 20,000 germs, but in a drop of putrefying fluid millions of bacteria may exist. Schimmelbusch reckons that the number of germs that settle upon a space a decimetre square amounts to about sixty or seventy during one half-hour's time in V. Bergmann's operating-theatre. In a cubic centimetre of the water of the river Spree, which flows past the clinic, it is estimated that there exist about 27,000 germs. Assuming, now, that a boatman should injure his hand, and should wait for half an hour in the clinic before it was dressed, he would receive upon the surface of the wound, covered probably with a blood-clot, from sixty to seventy bacteria. If, however, he undertook to "cleanse" the wound in the Spree water and to bind it with a dirty handkerchief, the number of organisms that would come in contact with the wound would amount probably to between thirty and forty millions.

It is evident that the danger of infection from the air has been very much overrated, and that operations may be performed with safety under conditions that were thought to be dangerous when Lister introduced the spray in order that the wound might be surrounded with a cloud of antiseptic vapor. When the spray was abandoned great attention was still given to the air of the room, and it is even now thought necessary by many to scrub the walls of a private apartment with antiseptics before an operation. The important point to remember is that the dust of the air should be allowed to settle, and that sweeping and cleaning should not be resorted to immediately before an operation.

The theory upon which the antiseptic treatment of wounds was based rendered it necessary that the wounded surface should be washed or irrigated with an antiseptic solution, in order to destroy all germs which might have found access to it during the operation. The spray destroyed those introduced with the air; irrigation destroyed those which were introduced through any other source.

It has been found, however, that bacteria may exist in an aseptic wound; that is, wounds may heal even though a certain number of organisms are present, the antiseptic properties of blood-serum and the vital energy of the cells being sufficient to prevent their development. These organisms may be found even after irrigation with a powerful antiseptic, such as 1 : 1000 solution of corrosive sublimate. Moreover, Halstead has shown that the irrigation of fresh wounds with 1 : 10,000 solution of corrosive sublimate is followed by a distinct line of superficial necrosis of the tissues, demonstrable under the microscope. Anything which interferes with the vital capacity of the tissues is, therefore, to be avoided. Welch dwells upon the importance of avoiding strong chemical disinfectants. Wounds should not be bruised nor made too tense, and spaces or foreign bodies that remove bacteria from the antiseptic action of the normal fluids of tissues of the body should not be allowed to exist. Experience has shown that the antiseptic treatment is open to certain grave objections, and this method has therefore during the last decade gradually yielded to that which is now known as the aseptic treatment.

Antiseptic irrigation led to active secretion of serum, and it necessitated drainage, but drainage-tubes were found to delay the permanent healing, being foreign bodies which favored the development of bacteria. With the abandonment of irrigation and the perfection of aseptic details drainage gradually became less necessary. The final step in the process of evolution from antiseptic to aseptic treatment was taken when the use of sponges moistened with an antiseptic fluid was abandoned, and dry sterilized materials alone were allowed to come in contact with the wounded surfaces. When it is necessary to wash away fragments of tissue and blood a sterilized salt-solution (0.6 per cent.) may be substituted for the antiseptic agents. Wounds thus treated cicatrize much more rapidly than those treated antiseptically. Antiseptic treatment cannot, however, wholly be discarded: it must still be resorted to when it is necessary to disinfect an infected wound.

It is now recognized that the *principal sources of wound-infection* are through contact with objects which are septic, such as the skin of the patient, the hands of the surgeon, and the instruments, sponges, sutures, and dressings. The secret of success in wound-treatment lies, therefore, in the completeness of the disinfection of these objects. Before considering the methods of disinfecting these different materials it may be well to study the action of some of the disinfecting agents. At one period the value of certain chemical substances as disinfecting agents was much more highly prized than at the present time. The essence of the antiseptic method consisted in the bactericidal action of these drugs.

Carbolic acid was first used by Lister, and it has had a long and a well-deserved popularity. It was found, however, to be much weaker in its germicidal action than corrosive sublimate, which was introduced later by Koch, and, when combined with oil, as it frequently was in the early days of antiseptic surgery, it was found to have little if any antiseptic action, as oil or grease protects the bacteria in a wonderful way from the action of germicides. Very strong watery solutions of carbolic acid (1 : 20) were found necessary to disinfect instruments and the hands, and the irritating action of such solutions upon the skin, as well as their disagreeable odor, was found to be a great objection to the use of this agent. Finally, the absorption of carbolic acid into the system through the skin, the mucous membrane, or wounds is attended by symptoms of poisoning that occasionally are alarming. The action of this drug upon the kidneys is occasionally well marked, and it is shown in all cases of absorption by the olive-green color of the urine. Many surgeons have been obliged to dispense with the use of this drug, owing to a peculiar susceptibility to its action. Carbolic acid possesses, however, a great advantage over corrosive sublimate in its power to penetrate greasy substances, and for this reason is often effective when the latter drug is powerless. Lister still lends the weight of his great authority to the use of this agent, and he employs it for disinfecting both the skin and the instruments.

When Koch first introduced *corrosive sublimate* his experiments showed that in the strength of 1 : 1000 it was able to destroy both the cocci and the bacilli in a few seconds. The experiments conducted by him consisted in treating a thread infected with various organisms with this agent, and in then placing it in a culture medium. Geppert showed, however, that washing the object with water before placing it in the medium was not sufficient to remove the antiseptic, and that consequently small quantities of the agent, being transferred with the disinfected object into the culture medium, hindered the growth of organisms and thus vitiated the experiment. In the case of corrosive sublimate it was found necessary to precipitate the mercury with sulphide of ammonium. Geppert found that under these conditions a 1 : 1000 solution of corrosive sublimate often failed to destroy the staphylococci.

Corrosive sublimate is therefore shown by these later experiments to be a much less powerful germicide than was originally supposed. It possesses also the great disadvantage that it is unable to penetrate the lumps of greasy dirt found under the nails and on the skin. It cannot be used as a disinfectant for instruments, owing to the corroding action of the mercurial salt. Finally, when used in strong solutions as an application to the skin or as a wash for wounds it is liable to produce poisoning. Salivation was not infrequent in the early days of its use, and dermatitis can easily be produced with the stronger solution. It is, however, still largely used as a disinfectant for the hands, and when combined with other means is exceedingly useful. The use of salt in corrosive-sublimate solutions prevents the precipitation of the sublimate in water. Corrosive tablets should therefore contain with the mercury an equal amount of salt.

Iodoform as a dressing of wounds was first employed about twenty-five years ago. It did not, however, come into general use until advocated by Von Mosetig-Moorhof. The freedom with which the powder was dusted into wounds led to cases of poisoning in which nervous symptoms were most marked. Under these circumstances iodoform can be detected in the urine. The best remedy is, according to Cutler, the administration of an alkali, as acetate of potash, and applications of powdered magnesia to the wound. The power of this drug as a germicide was first called in question by laboratory experiments, and the results did not agree with clinical experience. It is probable, as Jeffries first pointed out, that, while iodoform has no direct action as a germicide, it markedly retards the growth of bacteria and diminishes the foul odors of putrefaction. In the form of iodoform gauze it is a most valuable dressing for septic wounds. The drying effect of the powder is also an important factor in the prevention of bacterial growth. Owing to its poisonous action, iodoform may be replaced by aristol or dermatol (subgallate of bismuth) when it is necessary to use a drying powder freely.

The question of the air as a source of infection of wounds having been pretty thoroughly settled, attention was turned to the skin of the patient, the hands of the operator, and the various instruments and dressings which were brought in contact with the wounded surface. The *disinfection of the skin* has been a subject of much careful scientific investigation since it was known that the presence of the pyogenic cocci is so common in the epidermis. The investigations of Welch proved that a variety of these organisms called by him the "staphylococcus epidermidis albus" may be found even in the deep layers of the epidermis.

The localities in which the organisms seem to grow with the greatest activity are those where hair or the secretion of sweat is most abundant, such as the axillæ, the interdigital folds, the neighborhood of the scrotum, the navel, and the creases of the arms.

The part of the cutaneous surface requiring attention in every operation is the hands of the surgeon. It was supposed, when corrosive sublimate was introduced as an antiseptic agent, that washing the hands with a solution of this drug of a strength of 1 : 1000 was sufficient to sterilize the skin. Experience has shown, however, that no object which comes in contact with the wound is so difficult to clean as the hands. The fallacy in previous work of disinfecting the skin with corrosive sublimate consisted in neglecting to get rid of the antiseptic agent before subjecting the skin to the culture-test. Before placing the scrapings of the nails in an agar-agar solution the mercury should be removed from the hands by precipitation with sulphide of ammonium. Subjected to this test, corrosive sublimate is found to be quite ineffectual as an antiseptic, owing to its inability to penetrate the grease and the lumps of dirt in which the bacteria are imbedded.

Fürbringer has shown, however, that a preliminary washing with soap and water, followed by scrubbing with strong solutions of alcohol or of ether, enables one to remove the masses of dirt teeming with bacteria from beneath the nails and from other inaccessible regions, and that these preliminary washings are of more importance than the use of disinfectants. Such observations as these show that the mechanical removal of dirt is the most important feature of asepsis. The following are the principal features of the present German *method of rendering the hands aseptic* for a surgical operation : The hands are scrubbed energetically with a sterilized brush and soap for from one to five minutes. The hands having been wiped dry with a sterilized towel, the nails are thoroughly cleaned with a metallic instrument ; then the hands are rubbed for one minute in an 80 per cent. solution of alcohol or (in case special care is needed) with ether, and finally they are placed in a solution of corrosive sublimate (1 : 2000).

The following method, for a long time in use in the obstetric wards of many hospitals, has been shown recently by Welch to render the scrapings from the hands and nails perfectly sterile:

1. The nails should be kept short and clean.

2. The hands are washed thoroughly for several minutes with soap and water, the water being as hot as can comfortably be

borne and being frequently changed. A brush sterilized by steam or boiling is used. The excess of soap is washed off in water.

3. The hands are immersed for one or two minutes in a warm saturated solution of permanganate of potash, and are rubbed over thoroughly with a sterilized swab.

4. The hands are then placed in a warm saturated solution of oxalic acid, where they remain until complete decolorization of the permanganate occurs.

5. The hands are then washed off with sterilized salt-solution or with water that has been boiled.

6. The hands may then be immersed for two minutes in sublimate solution (1:500).

Bacteriological examination of skin thus treated yields almost uniformly negative results, the material for the cultures being taken from underneath and around the nails. If the hands have been in contact with septic material—as, for instance, during a demonstration on the cadaver—Park advises (after the use of soap, water, and brush) taking a tablespoonful or more of flour of mustard and washing the hands thoroughly with it as if it were powdered soap. Mustard is both a good deodorizer and a valuable antiseptic agent. The use of *sapo viridis* is a good substitute for the alcohol recommended in the German method of disinfection. It is a good material to place in the toilet-chamber of an operating-theatre when the hands must be cleansed repeatedly for operations following one another.

Many surgeons object to the use of the permanganate method of cleansing, owing to the difficulty of removing the stain from beneath the nails; but this can be effectually accomplished by an additional washing with peroxide of hydrogen. This agent should follow the oxalic acid, and after this series of washings the hands are spotless. One should always be careful to remove these powerful chemical agents from the hands by rinsing in sterilized water or in a weak antiseptic solution before placing them in a wound of the abdominal cavity.

The *preparation of the skin of the patient* may be facilitated greatly by a preliminary bath. When circumstances permit the preparation of the field of operation should be made the evening before. If the bath is not possible, a thorough local washing with soap and water should take its place. Those portions of the skin covered with hair—and indeed any part of the skin—should next be shaved with a razor, which instrument has been described by a French surgeon as an admirable dermal curette. Another most valuable instrument is the nail-brush, which should now be used freely with soap and hot water. In this way the grease which is natural to the skin is removed, together with the upper layers of the epidermis and the accompanying filth. Whatever remains may be removed by alcohol or by ether, as is customary in the German method of disinfection. When the skin has been prepared in this way the few bacteria which remain may be destroyed with a wash of corrosive sublimate (1 : 2000). It is rarely necessary to employ the permanganate-of-potash method already described, but a series of washings with chlorinated soda, ether, and peroxide of hydrogen may be used in unusually dirty regions. When it is necessary to get rid of a thick layer of filthy epidermis, as in the case of the feet of a laborer, a soft-soap poultice may be left on over night. The outer layer of skin then peels off and leaves the foot white as marble.

After the process is completed the surface of the skin may be covered with a corrosive poultice (1 : 5000), or fresh dry corrosive or sterilized gauze may be applied and not be removed until the moment of operation. On the scalp the hair must freely be removed, and if the brain is to be exposed the whole head must be shaved. Lister still retains faith in carbolic acid as a disinfectant for the skin, owing to its greater power of penetrating grease than corrosive sublimate. He does not even use soap and water, but considers a few minutes' action of a 1 : 20 solution of the acid sufficient. He does not approve of the practice of applying antiseptic lotions for hours together before an operation.

The long use of strong antiseptic washes is liable to irritate the skin and even to raise vesicles. It is better, therefore, to protect the part with an aseptic or a mildly antiseptic dressing in a dry state after disinfection.

The materials used during this process of preparation should be rendered thoroughly aseptic. It would be well to employ either an antiseptic soap or one prepared so as to be aseptic. The animal fat used in the preparation of soaps often contains large numbers of bacteria, and, if the soap is prepared by a cold method, it may abound in micro-organisms. If the materials are boiled during the process, this danger is avoided. *Sapo viridis*, or the combination of this soap with alcohol (soapy wash), is a most excellent substitute for the usual soap employed. The nail-brush should also carefully be attended to. Even when used for the disinfection of skin, nail-brushes have been found to contain many thousand bacteria (Schimmelbusch), and after the cleansing of the surgeon's hands, which may have been covered with pus, the condition of these brushes is of course highly septic. It is not sufficient to place the dirty brush in a strong solution of corrosive sublimate, as this agent may be unable to penetrate the greasy recesses. Boiling from one to five minutes in plain water or in 1 : 100 soda-solution is sufficient, however, to sterilize the brush. The brush should then be placed permanently in a 1 : 1000 solution of corrosive sublimate. Cheap brushes are prepared from wood-fibres, and they can be burned after using. A tender skin may not stand the ordeal of the brush. In this case the scrubbing may be done with gauze sponges.

The *disinfection of mucous membranes* is an extremely difficult problem, as they are usually highly septic, and the use of strong antiseptic washes may lead to poisoning. The employment of a 1 : 1000 corrosive-sublimate solution as a vaginal douche has repeatedly produced severe poisoning, and the same result has followed the use of carbolic acid, which is absorbed with great facility. According to Schimmelbusch, the only way in which a mucous membrane can be disinfected is by the mechanical removal of the dirt by scrubbing with sponges and by irrigation with warm water, or with sterilized salt-solution, or with weak solutions of boracic acid, or with permanganate of potash. It has been the writer's custom to use before operations upon the vagina a douche of corrosive sublimate not stronger than 1 : 10,000, or of carbolic acid not stronger than 1 : 400. Styrone, 1 : 100 or 1 : 150 solution, is an excellent disinfectant for the mouth (Beach). The use of salt in corrosive-sublimate solution prevents the precipitation of the sublimate in water. Corrosive tablets should, therefore, contain with the mercury an equal amount of salt.

Sterilization of Instruments.—Lister continues to use *carbolic acid* for sterilizing instruments. The instruments are placed in a 1 : 20 solution of carbolic acid just before the patient is brought into the room. They are kept in the solution during the administration of the anæsthetic, and they are then removed. There are, however, numerous objections to this method. Strong solutions of carbolic acid dull the knives and irritate the skin, and in some cases they may produce symptoms of poisoning of the operator or his assistant. This drug cannot be relied upon to penetrate the blood, the pus, the fragments of tissue which become imbedded in the crevices of the instruments, and therefore it is not available when instruments are to be used in several consecutive operations.

Dry heat is more effective than chemical disinfectants in its power to penetrate blood and dirt. Ordinary bacteria are killed in a few minutes, but the spores of anthrax bacilli are destroyed only after being subjected for three hours to a temperature of 140° C. In ordinary sterilizing apparatus great variations of the temperature are often found at different points. The steel instruments undergo molecular changes when subjected to very high temperatures, and they not infrequently become rusty. The process seems, therefore, to be too slow and uncertain, and it is liable to injure the instruments. Sterilization by steam can be effected in from fifteen to twenty minutes. Even this much shorter period is too long for ordinary purposes, and steam possesses the great disadvantage also of rusting the instruments unless they are managed with great care.

Boiling in water disinfects instruments in a few minutes, but there is the certainty also of rusting unless water is used which has been boiled for some time. This danger is, however, entirely obviated by the device of Schimmelbusch, which consists in adding 1 per cent. of bicarbonate of soda to the water (a heaping teaspoonful to the quart). The greater rapidity with which moist heat destroys bacteria is due to the solvent action of the moisture upon the material which surrounds and protects the organisms. This solvent action is greatly increased by the addition of the alkali, the fat, blood, and dirt being in this way much more readily removed from the instruments.

Boiling in water is the method which is, at the present time, almost universally employed. An ordinary fish- or asparagus-boiler is a suitable apparatus for the purpose. After removal from the boiler the instruments are laid upon a sterilized towel or they are placed in a 1 per cent. soda-and-carbolic-acid solution, in readiness for the operation. After use the instruments should be rinsed in cold water, to remove the blood, which would be coagulated by heat, and then thoroughly cleansed with soap and brush in hot water. Knives are apt to be dulled by boiling. They should therefore be washed thoroughly in soap and water, and then rubbed down with alcohol or sterilized gauze, or be placed for a few minutes in a weak solution of carbolic acid. They should carefully be polished after each operation, and should be frequently sharpened.

The three principal requisites demanded of the *surgical dressings* are—good absorbent qualities, freedom from pathogenic organisms, and an antiseptic action which will prevent the decomposition of the secretions of the wound. Although absorbent cotton can take up twice as much water as gauze, the latter material much more readily absorbs the secretions of a wound. Its porous character enables the thick, slimy fluid to filter through it. When only moderate secretion is expected and a small dressing is to be used, absorbent cotton is preferable, as it does not "stain through" so readily as gauze. Absorbent cotton, on the one hand, is useful, when moistened, as a sponge to cleanse the skin or to moisten the surface of a wound when the dressings are changed. On the other hand, gauze has replaced all other materials for sponge-work during an operation; pads of gauze neatly folded together, about two to three inches square, form a most useful substitute for the sea sponge. These pads after sterilization may be preserved in an aseptic condition for several days when carefully packed in an aseptic towel.

The question of the advisability of using antiseptic material in dressings is one about which there has recently been a great change of opinion. Large quantities of antiseptic dressings are manufactured which are supposed to possess germicidal properties. With the knowledge that has been gained of the action of the various antiseptics it is known that it is highly improbable that the chemical substance retained in these dressings can materially affect the growth of bacteria, particularly when they are protected by fatty or albuminous substances. Moreover, these antiseptic agents after a certain length of time undergo chemical changes which render them inert. Corrosive sublimate is a conspicuous example, and carbolic acid is greatly weakened in strength with the lapse of time. If the dressing is too strongly impregnated with the antiseptic agent, it may be extremely irritating to the skin of the patient. Finally, a careful bacteriological examination of the antiseptic dressings now prepared for the market has shown that they contain large numbers of micro-organisms.

The only antiseptic dressing that is generally relied upon at the present time when it is necessary to pack an infected wound is iodoform gauze. Although it is open to some of the objections above mentioned, there is no other form of dressing that prevents with such certainty the decomposition of the discharges from the wound. With the change from antiseptic to aseptic surgery has come the abandonment of the antiseptic dressing and the adoption of the sterilized dressing.

Sterilization of the materials used for sponges and dressings may be accomplished by dry heat, by steam, and by boiling in water. Dry heat possesses numerous disadvantages as a sterilizing agent. The spores of bacilli are destroyed only after being subjected three hours to a temperature of 140° C. It is, moreover, extremely difficult to keep the air of such an oven at a constant temperature, and a portion of the dressing materials is liable to become singed and brittle.

Boiling water will sterilize the materials placed in it in a few minutes, but this robs them of their dryness; it is precisely this quality of dryness which is valuable in a dressing, for there is no condition so unfavorable to the development of bacteria. A dry dressing favors the evaporation of the fluid portions of the secretion, and thus prevents bacterial growth. The old antiseptic dressing contained a water-proof layer which retained the moisture and favored growth of organisms, despite the antiseptic agents with which the wound was surrounded.

Steam may, however, be so brought to bear upon the materials to be sterilized as to reduce the moisture to a minimum. Steam acts also much more rapidly upon the bacteria than dry heat, as it penetrates more readily the micro-organisms. Superheated steam is too dry, and therefore is less effective. Steam under pressure is an exceedingly powerful disinfectant, but the apparatus necessary for this method is cumbersome and costly.

The methods of sterilizing with steam at present most in use are those adopted by Arnold and Lautenschläger. The Arnold sterilizer, so much used in America, employs steam under slight pressure. Materials placed in this apparatus are thoroughly sterilized after being subjected to a temperature of 100° C. for a half to three-quarters of an hour. The apparatus is simple and effective. The Lautenschläger sterilizer employs a current of slightly superheated steam so arranged that the steam enters the disinfecting chamber from above and is carried out from the bottom of the chamber through a tube. The dressing may be placed in these chambers either wrapped in towels or, better still, in perforated boxes so arranged that the perforations may be closed after the sterilization has been completed. The time for sterilization is about the same as that needed by the Arnold apparatus. Sponges or dressings loosely sewed up in cloths may thoroughly be disinfected, and be preserved for at least twenty-four hours in an aseptic condition, the wrapper acting like the cotton plug of a test-tube. The moist condition in which the materials are found when first removed from the sterilizer rapidly disappears: if the precaution is taken to warm the dressings first, the condensation which takes place when steam comes in contact with cold objects will be avoided.

Braatz devised a sterilizing apparatus which enables one to disinfect both the dressings and the instruments simultaneously. The chamber is so arranged that a tray containing the instruments in a soda-solution may be introduced, and the boiling process may then be carried on at the same time.

Ligatures may be prepared from silk or from catgut. *Silk* may be sterilized by boiling, and sutures may readily be prepared by boiling in soda at the same time with the instruments in the manner already described. Silk may be prepared beforehand by boiling for half an hour in water and preserving on glass or metal spools in 1 : 20 carbolic solution or 1 : 100 corrosive-sublimate solution (Schimmelbusch). Instead of water, steam may be used. The spools of silk may be placed in the sterilizer for three-quarters of an hour, and may subsequently be preserved in a special box or be sterilized in test-tubes corked with cotton. The dry sterilized thread is considered preferable to that preserved in an antiseptic solution.

Catgut was first prepared by Lister by placing the gut in a mixture of carbolic acid with ten parts of olive oil. Carbolized oil still continues to be used largely for the preservation of catgut ligatures, and the material thus prepared does not appear to cause any disturbance in the wound in the majority of cases. *Chromicized gut* was prepared by Lister for the purpose of procuring a more durable material. The gut is first placed in a 5 per cent. watery solution of carbolic acid which contains chromic acid in the proportion of 1 : 4000. The gut remains in this solution for forty-eight hours; it is then dried and preserved in 1 : 5 carbolized oil. These methods, when subjected to severe bacteriological tests, were found to be insufficient to produce an absolutely sterile gut.

Catgut is prepared from the sheep's gut by scraping away both the muscular and the mucous coats. The submucosa, a firm fibrous tissue, is thus left behind. The raw material not only teems with bacteria, but, when prepared in Europe, may also be made from the intestines of animals affected with anthrax. The spores of the bacillus anthracis are among the most durable of the spores of known organisms, and one or two cases of malignant pustule have actually been produced by the infection of wounds with the gut taken from diseased animals.

Braatz has shown that, next to the hands of the surgeon, nothing in surgery is more difficult to disinfect than catgut. The material purchased from the dealer is very greasy, and Braatz first showed that it was necessary to remove this grease in order to disinfect the gut properly with antiseptic agents. The new gut should therefore be placed for one or two days in ether. It should then be allowed to remain in 1 : 1000 watery solution of corrosive sublimate for twenty-four hours, and finally should be preserved in absolute alcohol. Bergmann prefers an alcoholic solution of corrosive sublimate, but Braatz showed experimentally that the watery solution is far more effective. By the addition of 20 per cent. glycerin to the alcohol the gut can be preserved in a more supple condition.

Attempts to sterilize catgut have generally been unsuccessful. Dry heat has been found the least harmful, but it requires an elaborately-prepared apparatus, in which the heat must be maintained at 150° C. for three-quarters of an hour. Brunner succeeded in sterilizing catgut by boiling in xylol. The spores of anthrax can be destroyed by boiling in this substance at a temperature of 100° C. for two and a half hours.

Catgut possesses the great advantage of being readily absorbed, and ligature sinuses are thus avoided. Although wounds are liable to reopen to allow the discharge of a silk ligature, silk is a safer material to use, so far as danger from hemorrhage is concerned, as catgut may soften and yield. It is a treacherous material.

Sutures may be made of silk, of silver wire, of catgut, or of silkworm gut. The method of sterilizing is essentially the same as in the case of ligatures.

Drainage.—The use of drains in aseptic wounds is now generally abandoned: long incisions, such as are made in removal of the breast with dissection of the axilla, may be united securely with sutures from one end to the other without fear, under strict aseptic precautions. In certain operations there is likely to be considerable oozing, such as in operations upon the brain; and there may be danger in closing a wound too tightly over the sensitive brain-tissue. Pressure is also to be avoided in operations upon the thyroid gland or on other large tumors of the neck, on account of the danger to the respiratory function. In such cases a small strand of sterilized or of iodoform gauze may be left in the corner of the wound for the first twenty-four or forty-eight hours. In deep or doubtful wounds, such as occur after operating upon the abdominal cavity, it may be necessary to use drainage-tubes. In such cases glass or rubber tubes may be used. Glass possesses the advantage of being sterilized easily by boiling, but it cannot always be provided in suitable lengths for a given case. Soft-rubber tubes are sufficiently stiff to preserve an open lumen under the ordinary pressure in a wound. They can be sterilized by boiling in water five minutes or by steam in fifteen to twenty minutes. They should be preserved afterward in 1 : 20 carbolic-acid solution. Corrosive sublimate is not suitable for this purpose, as it combines with the sulphur in the rubber and is precipitated.

Sponges have already been referred to in speaking of dressings. The gauze pad or loosely compressed pieces of sterilized gauze should be used for wiping up the blood in a wound. Sea sponges may, however, be needed occasionally, as in operations upon the mouth. The broad flat sea sponge is useful also in laparotomy to protect the intestines.

Billroth's method of disinfecting sea sponges is as follows: The sponges are thoroughly washed, and are then placed for twenty-four hours in a solution of permanganate of potash (1 : 500), and after that they are bleached in a 1 per cent. solution of hyposulphite of sodium to which has been added 8 per cent. of pure hydrochloric acid. They are then washed in water, and are preserved in 5 per cent. carbolic acid. According to Schimmelbusch, sponges are readily sterilized in boiling 1 per cent. soda-solution. This process shrinks them badly, but if the soda-solution is removed from the heater at the moment of placing the sponges in it, they are thoroughly disinfected after remaining half an hour in the solution. They should then be rinsed out in boiled water, after which they can be preserved in sublimate (1 : 2000), which is preferable to carbolic acid, as the latter drug discolors them. Sponges prepared in this way can, however, only be used a few times before losing their elasticity.

The directions already given cover most of the points needed to be observed in an aseptic operation. The coat of the operator, and the towels also, should be sterilized as carefully as the dressings when this is possible. Coat and towels can be carried in the bag or towel in which they have been sterilized to the house where the operation is to take place. If it is not possible to carry out these precautions, a clean sheet fresh from the laundry is sufficiently sterile for most purposes. The towels should, however, be wrung out in corrosive sublimate (1 : 1000).

During the operation it should be the duty of the surgeon to avoid bringing anything, except what is absolutely necessary to use, in contact with the surface of the wound. The fingers should touch the interior of the wound as little as possible, and the cuts of the knife should be made as clean and as straight as possible. Landerer has shown the importance of avoiding the use of wet sponges or of irritating fluids during the operation: these increase the local irritation and favor the exudation of serum. Dryness is therefore an important factor in preserving asepsis; it is also a valuable hæmostatic agent. The adoption of this method is a distinct advance in the modern method of treating wounds. It may, however, be necessary to use irrigation after a prolonged and bloody operation for the purpose of removing the blood-clot and of washing away the fragments of bruised tissue. In such cases boiled water may be used, or, better still, a sterilized salt-solution (.6 per cent.), which is absolutely neutral in its action upon the tissues. When there is a suspicion of infection having occurred during an operation, the wound must then be washed with an antiseptic solution, and corrosive sublimate is usually the best for this purpose, in a strength of 1 : 2000 or 3000. If weak antiseptics are used, such as saturated solutions of boracic acid, or weak solutions of strong antiseptic agents, such as ½ per cent. solution of carbolic acid, the water used should first be sterilized by boiling.

After the wound has been closed by sutures the line of the incision may be dusted with a drying powder, such as iodoform or aristol or dermatol. Such an application protects to a certain extent from the danger of stitch-abscess; but since the aseptic system has been perfected these precautions may be dispensed with. It is a valuable aid, however, to a dressing in moist regions, such as the axilla or the perineum.

In accidental wounds the first aid rendered should aim to be as antiseptic in its nature as circumstances will allow. The finger or the probe should not be introduced into the wound unless it has previously been rendered aseptic. The clot adhering to the surface of the wound may serve as a temporary protection, and it should not be washed away unless boiled water is at hand. A thorough washing of the wound with boiled water may be followed by the application of linen fresh from the laundry or of cloths that have been boiled for the purpose. Such a dressing may serve as a temporary expedient pending the thorough disinfection of the wound, which should be done as soon as possible. The first dressing cannot be too elaborately performed when means are at hand for the purpose. It is a well-recognized fact in hospital service that wounds heal badly just in proportion to the neglect of the initial treatment which they have received before the patient comes to the hospital. Every accidental wound should be treated as though it were infected. There are four indications for the emergency treatment of fresh wounds:

1. The removal from the wound of all visible dirt by means of forceps and thorough washing with boiled water.

2. The removal from the wound of microscopic dirt by means of flushing with boiled water and antiseptic solutions.

3. The prevention of subsequent infection.

4. The absolute immobility of the part.

Given a lacerated wound of the hand, the first step should be the cleansing of the skin in the immediate neighborhood of the wound. This is best accomplished by means of a solution of chlorinated soda, 1 part to 10 of water. The solution should be applied vigorously with the scrubbing-brush or a gauze sponge. Having cleansed the skin adjacent to the wound, the wound itself should also thoroughly be scrubbed with a gauze sponge or a scrubbing-brush wet in chlorinated soda. Shreds of tissue should be removed with the scissors. The hand should next be washed in peroxide of hydrogen to destroy all the dead organic material that may be in the wound or on the adjacent skin. The peroxide of hydrogen should be washed away with a solution of corrosive sublimate (1 : 5000), which in its turn should be removed by flushing the wound in boiled water. It is a not uncommon practice for the hospital interne to spend from one-half to three-quarters of an hour in this cleansing of the wound and the adjacent skin. If the disinfection of the wound has been complete, its subsequent infection may be prevented by the application of a sterilized dressing. The subsequent healing of the wound is favored and danger of infection lessened through immobilization of the part by the employment of a properly-applied splint.

APPENDIX.

A. Blood-serum Therapy in Rabies.

Centanni[1] gives a brief description of a method which he employed to render animals immune to rabies. Centanni's method consists in injecting into rabbits which have been inoculated with virulent rabies material a glycerin emulsion of the cord of an animal that died after inoculation with the so-called "fixed virus" of Pasteur. The emulsion is made as follows: 4 grammes of the cord are macerated in an artificial gastric juice for nineteen hours. [He does not say how much gastric juice is employed.] The fluid is then neutralized, and the precipitate is collected and dried over sulphuric acid. One-third of the precipitate so obtained was mixed with 5 cubic centimetres of glycerin. This emulsion was sufficient to prevent rabies in a rabbit when injected six days after the inoculation. Two control rabbits died on the seventeenth and eighteenth days, respectively.

Tizzoni and Centanni,[2] in continuation of work previously published as to the treatment of rabies by injecting the serum of animals immune to rabies, report results obtained by using a precipitate of the serum. The method employed is as follows: Blood-serum is obtained from rabbits rendered immune to rabies by the method of Pasteur. The serum is precipitated by the addition of ten times its volume of alcohol, and the precipitate is dried over sulphuric acid. In their experiments 1 gramme of the dried precipitate was sufficient to prevent the outbreak of rabies, though the injection had taken place eight days after the inoculation. All the control rabbits died in from eighteen to twenty days. Tizzoni and Centanni[3] give results of the treatment of rabbits with serum of large animals with the view of using the method in the treatment of human rabies.

[1] *La Reforma Med.*, 1892, Nos. 102 and 103.

[2] *Deutsch. med. Wochen.*, vol. xviii. p. 702.

[3] *Berliner klin. Wochen.*, No. 8, 1894.

B. Tetanus.

Schütz[1] gives an exact description of his method employed to render horses immune to tetanus. He injected bouillon culture of the tetanus bacilli, rendering the culture less virulent by the addition of trichloride of iodine. The first injection he made was one of 10 C.c. bouillon culture with 1 per cent. trichloride of iodine; on the second day, 12 C.c. bouillon with ½ per cent. iodine; and so on until finally, on the sixth day, he injected 26 C.c. bouillon with 0.2 per cent. iodine. The protective power of the serum is increased by injecting at intervals large quantities of a virulent culture into the animal after it has been rendered immune.

The antitoxine of Tizzoni and Cattani is prepared by treating the blood-serum of the immune animals with absolute alcohol. The precipitate may be kept dry or be preserved in glycerin. The dose of antitoxine averages 25 Cg.

C. Treatment of Cancer.

According to Willy Meyer, pyoktanin should be used in solution for parenchymatous injection in the strength of 1 : 500, although 1 : 100 solutions have been used. The solution should be kept in a dark bottle with a glass or a rubber stopper. Only a small quantity, about 1 ounce, should be prepared at a time. It is better prepared fresh for each injection.

In the beginning of the treatment of parenchymatous injection it is best to distribute the dye through the entire tumor as rapidly as possible. The injection should be made every other day or every third day, and should be made with strict antiseptic precautions. The needles must be boiled after using and then be kept in alcohol. The amount of the solution injected varies from ½ to 3 drachms.

In treating inoperable growths which are directly accessible, the needle should be pushed into the healthy tissues about one-third of an inch from the border-line, and then be conducted obliquely toward the base of the tumor.

For internal medication methyl-blue (Merck) is the preferable drug, as pyoktanin is not well borne by the stomach. The daily dose may be pushed up to 10 or 12 grains. The drug may be administered in gelatin capsules. The urine is colored at first a light green, and later a deep blue, by this treatment.

[1] *Zeitschift für Hygien*, vol. xii.

If the bladder be the seat of an inoperable cancer, Meyer recommends irrigation with pyoktanin, 1 : 1000 or 1 : 2000 or 3000, every third day. In treating inoperable cancer of the uterus the cancerous tissue should be removed with the curette, and the bleeding surface should be tamponed with dry iodoform gauze. Twenty-four or forty-eight hours later the gauze is removed and the treatment by injection is begun.

For external applications to ulcerating growths, also in cavities, as the vagina, a 1 to 2 per cent. creolin-pyoktanin solution (equal parts) is recommended. On ulcers of the face or the scalp the aniline dye is applied in the form of a salve, or dusted in as a powder, or rubbed on the surface with a moist pencil. The application of the pencil causes a crust or dry eschar to form, under which cicatrization takes place.

Roswell Park's solution of mercury, arsenic, and gold for the treatment of cancer contains the following ingredients:

℞. Hydrargyri iodidi rubri,	gr. viij;
Auri chloridi,	gr. xxiv;
Arsenici bromidi,	gr. xlviij;
Potassii iodidi,	gr. x;
Acidi nitro-hydrochlorici dil.,	ʒiiss;
Aquæ destillatæ,	ad ℥xv.

Preparation:

1st. Dissolve hydrarg. iod. rub. with potassii iod. in little water.

2d. Dissolve arsenic bromid. in a necessary quantity of water; heat gently.

3d. Dissolve gold chloride in just sufficient water to produce clear solution.

4th. Mix solutions of arsenic and mercury; apply gentle heat.

5th. Then add to the solution of mercury and arsenic the gold solution; heat gently and decant; set aside the clear portion.

6th. Add the acid to the precipitate slowly, and heat until clear solution results.

7th. Then add to this solution the decanted portion: a brown precipitate is formed. Heat until perfect solution results, and continue heat until the strong acid fumes have escaped and the liquid bumps. Then add distilled water to make fifteen ounces.

The solution should be of a saffron-red hue. It is given in 10-minim doses, each of which contains about $\frac{1}{15}$ grain of bromide of arsenic, $\frac{1}{30}$ grain of chloride of gold, and $\frac{1}{100}$ grain of bichloride of mercury.

D. Methods of Preparing Erysipelas Toxine.

The preparation at present used by Coley is as follows:

The streptococcus is grown in bouillon for two weeks: at the end of this time the bacillus prodigiosus is added, and the two allowed to grow together for ten days longer. The bouillon is then subjected to 58° C. temperature for one hour, and put in very small glass-stoppered bottles to which enough thymol has been added to make a saturated solution. This preparation is the most powerful yet obtained, and in doses of from .2 to .3 C.c. (♏ 2 to 4) has frequently produced a reaction temperature of 104° to 105° F. Its action upon sarcoma, and likewise upon carcinoma (though to a less degree), has been more marked than in any of the previous preparations used by Coley.

The toxines to be of value *must* come from a very virulent source. All of Coley's cases were treated with cultures obtained originally from a fatal case, and kept virulent by passing them through rabbits. The toxines should be kept in the dark and in a cool place. Frequent exposure to light and air lessens their strength. No death has attended the use of the toxines, and, carefully given, they may be considered free from danger. The preparation being sterile, permits its use in any general ward without isolation.

E. Spronck's method of preparing the erysipelas toxine is as follows:

Plant two flasks of bouillon with a virulent culture of erysipelas. Seal the flasks, and allow them to remain for two weeks at a temperature of from 33° to 35° C. At the end of that time cover-glass preparations should be taken to test the purity of the growth.

To one flask Spronck adds 5 per cent. of glycerin, and he evaporates this mixture by boiling, so that it is reduced to one-tenth its original volume. This residue is added to the other flask, and the mixture is filtered through a Chamberland filter.

(The fluid thus obtained should be proved to be sterile by control experiment).

Spronck thus obtains a glycerin extract of the bacterial proteids in the first flask, and in the second flask also the toxines which are destroyed by the heat in the first flask.

E. Examination of Tumors.

Hardening in Alcohol.—For rapid examination of specimens the tumor should be cut into very small pieces, which should be placed in a large amount of absolute alcohol. Scrapings from the uterus may be rolled up into a ball, and then be put into alcohol, thus solidifying them into a mass which can be mounted in celloidin and be cut like a solid section.

Large pieces of tumors or other tissues can be placed in 70 per cent. alcohol, which is changed at first every day, then every other day, the strength of the alcohol being gradually increased until finally strong 95 per cent. alcohol is used. In this fluid they can be left for future use.

Müller's fluid consists of:

Bichromate of potash,	2 parts;
Sulphate of soda,	1 part;
Distilled water,	100 parts.

The fluid should be changed frequently at first, several weeks to several months being required for hardening.

Paraffin-mounting Method.—Cut the hardened specimen into small pieces, the smaller the better.

I. Absolute alcohol, from four to twenty-four hours.

II. Oil of cloves and xylol, equal parts, from four to twenty-four hours; better to use two changes.

III. Paraffin melting at 54° to 55° C. Use two or three changes, to get rid of all the oil of cloves; in all, from four to twenty-four hours.

IV. Mount and place in cold water.

To get Rid of the Paraffin.—(1) Place the sections in xylol for several minutes, using two or three changes if there are many sections; (2) absolute alcohol; several changes if necessary; (3) alcohol 95 per cent. The sections are now ready to stain.

Imbedding in Celloidin.—After hardening, cut into small pieces for mounting.

1. Absolute alcohol for twenty-four hours.
2. Absolute alcohol and ether, equal parts, twenty-four hours.
3. Thin celloidin, from twenty-four hours to two weeks.
4. Thick celloidin, from twenty-four hours to two weeks.
5. Allow to evaporate in a covered dish for several days until of firm consistency; then cut the specimens out and mount on blocks with thick celloidin. Let them stand from five to ten

minutes exposed to the air, then place in from 70 to 80 per cent. alcohol, and cut after twenty-four hours.

Perfect hardening takes place rather slowly, though taking place more rapidly when the temperature is kept between 30° and 40° C. The fluid should be changed frequently. After hardening, the specimens should be kept in 80 per cent. alcohol until wanted for mounting.

F. Staining Methods.—*Tumors.*

Gage's Hemotoxylin.—1. Place the section in water to remove alcohol.

2. Stain two to three minutes until light blue.

3. Wash thoroughly in water (two changes), or, better, soak for half an hour in a large amount of water.

4. Alcohol, two changes, stirring round.

5. Alcoholic solution of eosin, ½ to 1 per cent., one or more minutes.

6. Wash off excess of eosin in alcohol.

7. Clear in oil of bergamot (or oil of cloves).

9. Mount in xylol balsam.

G. So-called Parasites of Cancer.

For hardening specimens of cancer to show the presence of the so-called "parasites" alcohol has been abandoned, as alcoholic specimens frequently do not show the desired picture, while parts of the same cancer, hardened by different methods, reveal them in large numbers. The specimen should therefore be placed in a solution of 1 per cent. osmic acid for twenty-four hours, and then transferred to 80 per cent. alcohol for several weeks. The specimen is mounted in celloidin or paraffin for cutting, and the sections are stained with eosin and hæmatoxylin.

The specimen may also be hardened in Foa's solution, which consists of a saturated solution of corrosive sublimate in 75 per cent. salt-solution and 5 per cent. potassium bichromate, equal parts.

When the specimen is thus hardened the section should be stained with eosin and aniline-blue.

Another hardening fluid is Flemming's solution, which consists of

2 per cent. watery solution of osmic acid,	4 parts.
1 per cent. watery solution of chromic acid,	15 parts.
Acetic acid.	1 part.

The specimen is kept in this solution for from one to three days. It is then washed in water for from three to six hours, and placed in from 30 to 95 per cent. alcohol, which is changed at intervals of several days.

H. Decalcification of Bone.

Bone should be sawed into very small pieces, and then be placed in the decalcifying fluid, which is prepared as follows:

Phloroglucin,	1 Gm.
Nitric acid (C. P.),	10 C.c.

These should be mixed, and then 90 C.c. of 10 per cent. nitric acid is added.

This fluid is a dark red-brown, which changes to a light yellow on exposure to the light and air. The pholoroglucin protects the cell-elements from destruction by the nitric acid. Decalcification should take place in from one to three hours. When decalcified, the bone should be placed in alcohol, and when the acid has been removed it may be put in celloidin and mounted.

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