MANUAL OF BACTERIOLOGY AND PATHOLOGY

FOR NURSES

BY

JAY G. ROBERTS, Ph. G., M. D.

OSKALOOSA, IOWA

ILLUSTRATED

PHILADELPHIA AND LONDON

W. B. SAUNDERS COMPANY

1914

Published August, 1912. Reprinted November, 1912, and January, 1913

Reprinted June, 1914

PRINTED IN AMERICA

PRESS OF
W. B. SAUNDERS COMPANY
PHILADELPHIA

TO MY MOTHER
THIS BOOK IS AFFECTIONATELY
DEDICATED

PREFACE

THIS work is the result of several years experience in teaching the subjects of bacteriology and pathology to nurses. It was early discovered that there did not exist any work on these subjects which seemed adapted to the peculiar requirements of the busy nurse in training or in practice. The fact that such a work must of necessity be brief has been recognized, but a constant effort has been maintained to avoid sacrificing accuracy or lucidity for brevity. Considerable space has been devoted to the subjects of infection and immunity and to bacterial and serum therapy, because it was realized that the trained nurse, because of her intimate and continued association with them, is to become the great teacher of the masses in the newer developments in medicine and sanitation, as the physician can never be, and she should, therefore, keep abreast of the times on these subjects.

The subjects of microscopic diagnosis and pathologic technic have not been entered into to any extent, as they are of interest only to those nurses who contemplate be-

coming surgical or bacteriologic assistants, and such are referred to the more pretentious works for physicians.

Physicians returning from abroad almost universally remark upon the superiority of the nursing in most American hospitals. If this be true, and, as is generally believed, it be due to the greater amount of time and attention devoted to the training-schools for nurses by American physicians, it is the earnest hope of the author that this little book may aid in some small measure in maintaining this enviable position of the American trained nurse.

In conclusion, I wish to thank the students of the Oskaloosa Training School for Nurses for the encouragement which their appreciation of the lectures upon which this book is based has given me, and, finally, to express my deep obligation to my wife, who has aided and encouraged me in many, many ways in the preparation of this work, especially in revising and transcribing the manuscripts and in correcting the proof sheets.

J. G. R.

OSKALOOSA, IOWA.

CONTENTS

BACTERIOLOGY

PATHOLOGY

CHAPTER XVI

CHAPTER XVII

CHAPTER XVIII

CHAPTER XIX

CHAPTER XX

CHAPTER XXI

CHAPTER XXII

CHAPTER XXIII

CHAPTER XXIV

BACTERIOLOGY AND PATHOLOGY FOR NURSES

BACTERIOLOGY

INTRODUCTION

THE story of the development of the science of bacteriology reads like a romance. For untold ages man struggled blindly and desperately with an unseen foe. Struggled helplessly and afraid, because of the nature of this dread adversary he knew nothing; he could neither see, hear, nor feel it; it came and went like a specter in the night, and man knew it only by the havoc it wrought, and he measured its power by the dead bodies of its victims. Wild beasts and poisonous snakes he had conquered; heat and cold, storm and calm, mountains' heights and oceans' depths he had learned to circumvent, or had made to minister to his needs; but still this silent, invisible foe stalked up and down the face of the earth exacting its grim toll of life and health.

Groping blindly, man learned some things about this unseen enemy. He learned that it sometimes infested the food that he ate or the water that he drank, but he

knew not how nor when. He learned that those who were seized upon by this foe were a source of danger to others, as were likewise their clothing and their houses. In other words, he learned that diseases were contagious, but how or why he knew not.

For ages the leper had been considered "unclean," and since the dawn of the world of man had plague-infested cities been shunned, and, later, those who were afflicted and their habitations were purified by baths and smudges and noxious fumes.

Then an observing Dutchman of an inventive turn, Leeuwenhoek, of Delft, about the year 1680 produced a lens of such power that this enemy of man could be seen, though it was not recognized as such at that time. Though Leeuwenhoek certainly discovered the existence of bacteria and described them, neither he nor any one else succeeded in connecting them with disease for nearly two centuries. So for two hundred years, though its presence was known and its guilt ofttimes suspected, the disease germ remained unconvicted.

Oliver Wendell Holmes, an American physician-author, in 1843 suspected the cause of puerperal fever and wrote on its contagiousness. In reply to the criticism and invectives which were heaped upon him because he ventured so new and astonishing an idea in medicine he wrote:

"It is as a lesson rather than a reproach that I call up the memory of these irreparable errors and wrongs;

no tongue can tell the heart-breaking calamity they have caused; they have closed the eyes just opened upon a new world of love and happiness; they have bowed the strength of manhood into dust; they have cast the helplessness of infancy into strangers' arms or bequeathed it, with less cruelty, the death of its dying parent. There is no tone deep enough for regret and no voice loud enough for warning. The woman about to become a mother or with her newborn infant on her bosom should be the object of trembling care and sympathy wherever she bears her tender burden or stretches her aching limbs. The very outcast upon the streets has pity upon her sister in degradation when the seal of promised maternity is impressed upon her. The remorseless vengeance of the law, brought down upon its victim by a machinery as sure as destiny, is arrested in its fall by a word which reveals her transient claim for mercy. The solemn prayer of the liturgy singles out her sorrows from the multiplied trials of life, to plead for her in the hour of peril. God forbid that any member of the profession to which she trusts her life, doubly precious at that eventful period, should hazard it negligently, unadvisedly, or selfishly."

In 1847 Semmelweis, of Vienna, forged a link in the chain of evidence which was at last to demonstrate the identity of this unknown foe and give man a fighting chance for life. Semmelweis noted a high rate of mortality for puerperal fever in a hospital ward, the attend-

ants of which were in the habit of coming direct from the dissecting room to the care of patients in confinement.

Observing the similarity between puerperal fever and a case of pyemia caused by a dissection wound, he suspected their identity, and the dissection room as their origin. He introduced a rule providing that all attendants from the dissection room must cleanse their hands with soap and water and chlorin solution, to "kill" the suspected poison, before they were allowed to attend the confinement cases. The results were immediate and astonishing. The cases of puerperal fever were far below the average for that period among cleanly midwives and attendants.

But it was in the study of fermentation that the connection of bacteria with disease was finally demonstrated. Pasteur, working with fermentation, discovered its bacterial origin, and in 1869 demonstrated that a disease of silk-worms was due to bacteria. Lister, in 1867, concluded that suppuration in wounds was a form of fermentation and could be prevented as could fermentation. His results from the application of aseptic and antiseptic methods in surgery, which methods he originated, supported his conclusions, and he is known to-day as the "Father of modern aseptic surgery." Davaine, in 1863, produced anthrax in animals by injecting them with blood containing anthrax bacilli from animals having the disease. This, however, did not prove the bacillus to be the cause, as there might

be other substances in the blood which caused the disease.

In the late seventies Pasteur and his pupils reproduced anthrax in animals from a pure culture of anthrax bacilli grown outside the body of an animal, thus confirming Davaine's observations and settling the question of the cause of anthrax. Koch, in 1882, discovered the tubercle bacillus and proved it to be the cause of tuberculosis.

Jenner, a hundred years before, had produced immunity to small-pox by inoculating with a modified form of the disease cow-pox; and Pasteur, now working along similar lines, produced immunity to anthrax by inoculating animals with a culture of the germ which had been attenuated by heating. Behring, in 1893, produced diphtheria antitoxin, and the beginning of the end of the conflict of the ages was apparent. Flexner has produced a curative serum of great value in cerebro-spinal meningitis, and vaccination against typhoid fever is proving very valuable in the armies of the world. In view of the progress made in the establishment of immunity in the last twenty-five years, it is not too much to expect that the middle of the twentieth century will see the production of immunizing agents for practically all infectious diseases.

CHAPTER I

DEFINITION, MORPHOLOGY, AND PHYSIOLOGY

Bacteriology is the study of micro-organisms, especially in their relation to health and disease.

Bacteria, microbes, micro-organisms, or germs are practically synonymous terms, designating the lowest form of plant life of the class fungi. They are minute single-celled organisms composed of protoplasm, nuclear chromatin, and surrounded by a cell wall containing cellulose or an albuminous membrane. In size they average 1 mmm. in diameter and may, therefore, only be seen by means of the high-power microscope.

Form.—Bacteria are classified according to their shape as follows:

Bacilli, cylindric or rod-shaped organisms.

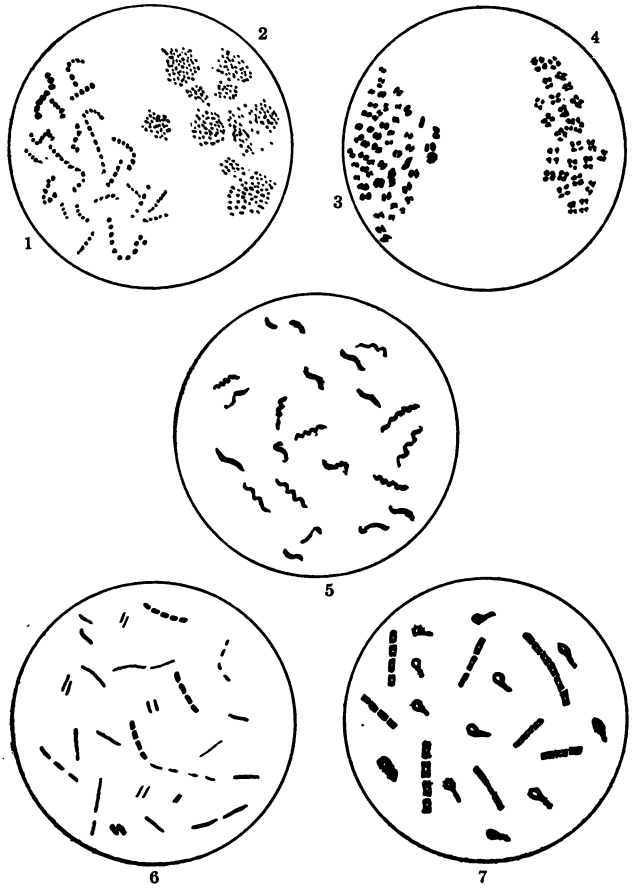
Spirilla, curved or spiral rods.

Cocci, spheric or globular organisms.

Flagella.—Attached to many bacteria are found fine thread- or hair-like projections, termed flagella, which keep up a constant movement. They are doubtless organs of locomotion, as they are found most frequently in motile bacteria.

Motile bacteria are those forms which possess the power of moving themselves from place to place.

PLATE I



Various forms of microörganisms: 1, Streptococci; 2, staphylococci; 3, diplococci; 4, tetracocci; 5, spirilla; 6, bacilli; 7, bacilli with spores (Paul).

Non-motile bacteria are those forms which do not possess the power of locomotion.

Reproduction.—In common with all living organisms, bacteria possess the power of reproducing their kind and in keeping with their uncomplicated structure; their mode of reproduction and multiplication is correspondingly simple, namely, by fission or simple transverse division.

Fission, the process of bacterial reproduction, takes place as follows: The cell elongates, an indentation occurs in its wall, which gradually increases in depth until the cell is completely divided, and two cells take the place of one.

Sporulation.—Under certain conditions of heat, light, oxygen, etc., conditions detrimental to bacterial activity, there occur in some bacteria glistening, highly refractive bodies termed spores. These are surrounded by a tenacious membrane or capsule, and when the spore is fully developed the remainder of the bacterium disintegrates and disappears. These bodies are supposed to represent the seed or resting stage of the plant's existence and is a means whereby the organism resists deleterious influences. It is not, however, a means of multiplication as in the higher plants, as each bacterium produces but a single spore, which, under favorable conditions, again develops into a complete bacterium, which may multiply in the usual manner by division.

Owing to the tenacious character of its membrane the

spore is much more resistant to the action of heat, light, antiseptics, and other injurious agencies than are the fully developed organisms. They resemble in this respect the seed of more highly organized plants which withstand conditions which are rapidly fatal to the growing plant.

CHAPTER II

CONDITIONS FOR GROWTH AND PRODUCTS OF THE GROWTH OF BACTERIA

Soil.—Bacteria differ in their selection of material upon which they grow: some preferring dead organic matter, others living only on the tissues of living organisms. Some grow well on either soil.

Saprophytes are those bacteria which grow on dead organic matter; for this reason they must be looked upon as benefactors to the human race. It is through their action that dead bodies and other highly complex organic materials are broken up into simpler forms and reduced to the dust from whence they sprang; thus is the earth rid of its carrion, and at the same time vegetation, upon which man and the higher animals subsist, is furnished with the simpler compounds of nitrogen, hydrogen, carbon dioxid, ammonia, and water necessary for its growth.

Parasitic bacteria live upon living tissue of man and other animals, and must, therefore, be looked upon as foes of mankind.

Pathogenic bacteria are those bacteria which produce disease. Inasmuch as practically all parasitic bacteria

produce disease under certain conditions, the name pathogenic bacteria is practically synonymous with parasitic bacteria.

Non-pathogenic bacteria are those which do not produce disease, and are, for the most part, saprophytic.

Stains.—Different germs behave differently toward various pigments when brought in contact with them. Advantage is taken of this fact in diagnosis, germs being differentiated in many cases by their staining or failing to stain with a certain stain. It also assists in recognizing their presence in tissue sections.

Temperature.—Some bacteria grow and multiply at a temperature as low as 0° C. (32° F.), while others flourish at 70° C. (158° F.). Pathogenic bacteria thrive better at about the temperature of the human body. While cold stops the growth and multiplication of these forms, it is destructive to but few of them. Higher temperatures they do not endure so well, and a temperature of 60° C. (140° F.) for a prolonged period is destructive to the majority of forms. A much higher temperature for a short time may be harmless, and freezing and thawing several times is destructive to very many forms. Spores, as mentioned before, withstand greater degrees of either heat or cold than the bacteria themselves.

Moisture is absolutely necessary to the growth and multiplication of bacteria. Drying is fatal to a few forms, as the cholera spirillum, but merely prevents the growth of the majority of species.

Food.—Because of the absence of chlorophyll the majority of forms of bacteria are unable to obtain their food-supply of carbon and nitrogen from the air as do higher plants, but must obtain it from the organic matter on which they grow, as the tissues of animals or the more highly organized plants. So it is that when bacteria are grown artificially, it must be on substances containing these necessary food elements, as gelatin, blood-serum, animal matter, or agar-agar and potatoes, highly organized plant matter.

Oxygen.—Different bacteria differ in their behavior toward oxygen.

Aërobic bacteria are those which cannot exist without the presence of oxygen.

Anaërobic bacteria are those to whom oxygen is fatal.

Facultative bacteria are those which can exist either with or without oxygen. Those thriving best with oxygen, but which can exist without, are called facultative aërobes, while those thriving best without oxygen, though existing with it, are termed facultative anaërobes.

Light.—Direct sunlight and strong electric light are both fatal to most bacteria, hence the importance of an abundance of sunlight in buildings designed for human habitation.

Products of Bacteria.—The products of bacterial growth are varied and complex. Some produce acids, as the butyric and lactic acid produced respectively by the Bacillus butyricus and Bacillus acidi lactici, and

the production of acetic acid in the manufacture of vinegar. Others still produce gases and odors, some fragrant, others foul and noxious, as in the putrefactive processes.

Poisons.—Just as certain plants of the higher orders, such as nux vomica, nightshade, and others, produce substances which are poisonous to animal organisms, so do these lower plant forms of bacteria produce poisons which in many instances closely resemble the poisonous alkaloids of the higher orders of plants.

Ptomains.—Certain of the complex alkaloidal poisons produced by saprophytic bacteria in their growth on dead organic matter are called ptomains. The ingestion of food containing these poisons may result in illness or even death.

This is doubtless the only exception to the rule that saprophytes are benefactors of mankind. In their zeal to rid the earth of organic matter saprophytic germs often attack food-stuffs which man has not yet abandoned. Upon the ingestion of meat, shell-fish, eggs, milk, and other foods wherein such bacterial activity has taken place ptomain-poisoning results.

Toxins.—The products of parasitic bacteria are termed toxins, and to these poisonous substances are due most of the pernicious effects of bacterial activity in the animal body.

Nearly all the changes in the organs of an animal caused by bacterial disease can be reproduced by injec-

tion of the toxins of the causative germ, and in many instances most of the symptoms of the disease may be so reproduced.

Protozoa are minute unicellular animal organisms closely allied to bacteria, but differing from them in their mode of reproduction. They pass through a complicated life-cycle which has been followed completely only in the malarial protozoa. There occurs first an asexual cycle or reproduction which takes place in man, wherein each parasite breaks up into six to twenty spores or daughter-cells, which rapidly develop into full-grown parasites. The periods of chills, fever, and sweats of malaria correspond to these periods of reproduction of the parasite. Then there occurs a sexual cycle which takes place in an intermediate host, the mosquito. Male and female elements are represented in this cycle and a peculiar spore formed, which, when injected into man, develops into the complete organism and proceeds to pass through the asexual cycle again.

CHAPTER III

INFECTION, SUSCEPTIBILITY, AND IMMUNITY

Infection is understood to be the introduction into an organism of a disease-producing germ, followed by the growth and development of the germ, and the production of the characteristic effects of the growth and development of that germ upon the infected organism. From this it follows that every introduction of a germ into an organism does not constitute infection, inasmuch as disease does not always follow such introduction. Before disease can be produced by the introduction into an organism of any particular germ certain conditions must exist. In other words, the organism must be susceptible to the disease and the germ must be virulent.

Susceptibility.—By susceptibility is meant the ease or difficulty with which a germ develops upon a certain organism. Thus, children are more susceptible to measles, scarlet fever, and whooping-cough than are adults.

Immunity.—The term immunity is used to describe the condition of absolute lack of susceptibility. If an animal is so constituted that the germ of a disease will not grow upon his tissues or that the toxins of that germ are harmless to the animal, the animal is immune to that particular disease. Thus, man is immune to hog cholera,

symptomatic anthrax, and hen cholera, while all animals except man and monkeys are immune to syphilis.

Such immunity is termed *natural immunity* in contradistinction to *acquired immunity*, which is exemplified in the immunity which follows an attack of some infectious disease, as measles, scarlet fever, and whooping-cough, and may also be produced artificially by vaccination, injection of antitoxin, etc.

Vaccination.—In vaccination the subject is infected with an attenuated or modified form of the disease which, however, is sufficient to give immunity to further attacks. Jenner, by infecting individuals with cow-pox, which is a modified form of small-pox caused by the growth of the small-pox germ on an unfavorable host, the cow, procured immunity to small-pox. Pasteur produced a vaccine against anthrax by subjecting an anthrax culture to high temperature for twenty days, thus so destroying its virulence that an animal infected with such a culture had a very mild attack of anthrax, which, however, was sufficient to render it immune to further attacks of anthrax.

Bacteriolysis.—It has been found that normal blood-serum possesses the power to destroy bacteria under certain conditions. This property is termed bacteriolysis. Various substances in the serum are concerned in such destruction, such as alexins, lysins, etc. Just what part each and every one of these substances play in bacteriolysis is not as yet definitely known.

Agglutinins.—There is found in the blood-serum of animals suffering from certain diseases substances which, when such serum is added to a liquid culture of the germ of that disease, cause a clumping together into a motionless mass of the bacteria of the culture. Advantage is taken of this in the so-called Widal test for typhoid fever, which will be described later.

Phagocytosis.—Metchnikoff in his studies discovered that certain body cells, chiefly the polynuclear leukocytes, possess the power of surrounding and ingesting foreign substances, such as carbon, dust, and other foreign bodies inhaled or driven into the tissues by injury, also bits of degenerated or dead tissue, and, most important of all, bacteria. These cells he called phagocytes and the process phagocytosis.

Metchnikoff believed that recovery from disease and subsequent immunity depended on the ability of the phagocytes to destroy the invading bacteria, and that when the phagocytes were unequal to the task the bacteria conquered and death ensued. It was found, however, that in some instances the leukocytes failed to attack the invading germ. Bail found this to be due partially to certain products of bacterial activity which he termed

Aggressins, the property of which seemed to be to render the bacteria more aggressive, while paralyzing or checking the activity of the phagocytes.

Opsonins.—Wright and Douglas in 1903 found that

phagocytosis depended upon the presence in the blood of substances which they called opsonins, which so act upon live bacteria as to make them fit food for the phagocytes, thus producing just the opposite effect from that of the aggressins. They found that these opsonins differ for the different varieties of bacteria, that an opsonin for one variety of germ had no effect upon germs of another variety.

Bacterial Vaccines.—They further found that by injecting dead cultures of a germ the opsonins for that germ were increased, and phagocytosis stimulated accordingly. These dead cultures prepared for such use were called bacterial vaccines.

Antitoxin.—When any plant organism grows on a certain soil for any length of time it produces substances detrimental to its own life and growth. The farmer recognizes this in his rotation of crops. So bacteria grown too long on the same artificial media cease to flourish and even die. In the animal body this doubtless occurs, but of more importance is the fact that there are produced by the body cells antibodies or substances antagonistic to bacterial growth and antidotal to their poisons. Whether produced by the phagocytes or by the fixed tissue cells, or by both, is not definitely known, nor is it important to us. The fact remains that there is produced in the course of certain diseases certain substances called antitoxins, which may be recovered from the blood of the animal which has been the subject of the

disease, and which may be introduced into the blood of other animals suffering from this same disease, where they unite with the toxins of the disease, rendering them harmless. At the same time they so affect the causative germ as to check its growth, or else the germ exhausts its soil or is attacked by the leukocytes, which are no longer paralyzed by the toxins and aggressins; at any rate, its activity ceases and recovery occurs. The most important antitoxins are those of diphtheria and of tetanus, of which more will be said later.

Theories of Immunity.—From the contents of the foregoing pages it will be gathered that several theories have been adduced in explanation of the phenomenon of immunity.

It will doubtless eventually be found to depend upon the presence in the blood of these wonderful substances, opsonins and antitoxins, either alone or in combination. It is a fact already known that the injection of antitoxin renders an individual immune to diphtheria for a greater or less period of time, and raising the opsonic index by vaccination against typhoid fever has been practised with great success, rendering the vaccinated individual immune to the disease in some instances for years. It may be that in some diseases the immunity is the result of phagocytosis, while in others it is due to the antibodies, or, perhaps in some, a combination of both.

CHAPTER IV

EXAMINATION OF BACTERIA, MICROSCOPIC DIAGNOSIS, ETC.

INASMUCH as only those nurses who become surgical assistants or laboratory workers will be concerned in the details and specific methods of bacterial examination and technic, no attempt will be made here to present such methods in detail. Those who are interested in such laboratory technic are referred to the more pretentious works for physicians and medical students.

Owing to their minute size, bacteria can only be examined by means of a high-power microscope, assisted by a device known as an oil-immersion lens, in which a drop of cedar oil is interposed between the lens and the cover-glass, beneath which is the object to be observed, the purpose of such device being to concentrate all of the rays of light emerging from the specimen observed. In addition there is needed an Abbé condenser, a device for concentrating the rays upon the object viewed.

Being provided with the proper apparatus, the specimen may be examined in several ways. If the specimen be from a liquid culture, a drop may be taken on a platinum loop placed between a cover-glass and slide

and examined with the oil-immersion lens. Or it may be examined by the hanging-drop method. In this method a slide is used in which a small depression is hollowed out. The drop of culture or pus to be examined is placed upon the cover-glass, which is then inverted over the depression, and the drop allowed to hang free in the space between the cover-glass and slide. By this means the movement of motile bacteria and agglutination, as in the Widal test, may be observed. By sealing the edges of the cover-glass, evaporation is prevented, and the specimen may be studied for days, and such processes as spore formation and fission observed.

If it be desired to stain the specimen, it must be prepared in the form of a *smear*. A small amount of the material is taken on a platinum loop (if liquid) or needle (if solid) and smeared over the surface of a cover-glass. It is then *fixed* by being passed through an open flame, thus coagulating the albumin of the material and fastening it to the cover-glass. The proper staining fluid is then flowed over the smear and allowed to remain the required length of time, with or without the application of heat, according to the stain used and the specimen examined. When stained, it is placed upon a slide with a drop of water interposed, or if it be desired to mount the specimen permanently, a drop of Canada balsam is used instead of the water between the cover-glass and slide, and the specimen examined in the usual manner.

If the specimen to be examined be tissue, a complicated process of hardening and embedding in paraffin or celloidin must be carried out, after which sections or slices so thin as to be translucent are cut from the specimen, the paraffin or celloidin dissolved out, and the section stained by immersion in solutions of certain dyes. It is then mounted in Canada balsam and examined in the usual way.

CHAPTER V

BACTERIA IN DISEASE

ATTENTION has already been called to the rôle played by saprophytic bacteria in ridding the world of the dead bodies of plants and animals. Mention may also be made of the use made of bacteria in the industries, as the bacillus whose growth in cream imparts the agreeable flavor to butter and cheese, the bacteria used in the manufacture of vinegar; even in tilling the soil advantage is now taken of the property of nitrifying bacteria to extract nitrogen from the atmosphere to enrich the soil and take the place of chemical fertilizers.

But to the nurse the most important thing in connection with the whole subject of bacteriology is the part played by bacteria in the production of disease. By far the greater number of diseases to which the animal world is heir are due to bacteria, and even the vegetable is not exempt, and has its germ diseases.

Koch's Rules.—Koch laid down certain rules which he held must be complied with to prove that any bacterium was the cause of any particular disease:

First: It must be found in the tissues or secretions of the animal having the disease.

Second: The germ from the affected animal must be grown in pure culture on artificial media.

Third: Such culture should produce the disease when introduced into a healthy animal.

Fourth: The same organism must be recovered from the tissues or secretions of the animal thus infected.

Infectious Diseases.—Any disease caused by the growth and multiplication of a micro-organism on the tissues of the animal having the disease is called an infectious disease. Not all infections are due to bacteria, since malaria and yellow fever are due to minute animal organisms.

Contagious Diseases.—A disease which is acquired by direct or indirect contact with an individual having the disease is termed a contagious disease. All contagious diseases are infectious, but not all infectious diseases are contagious. The distinction is more apparent than real and is not important.

Avenues of Infection.—The embryo may be infected, though rarely, through the ovum or the spermatozoa. Infection with syphilis may thus occur. The fetus may be thus infected through the placenta with small-pox, scarlet fever, tuberculosis, etc., when the mother suffers from the disease. Bacteria may gain entrance to the body through the healthy skin in rare instances; usually it is through minute wounds of the skin. The mucous membranes of the mouth, nose, throat, bronchi, ali-

mentary canal, urethra, vagina, etc., offer less resistance than does the skin to the passage of germs.

After introduction the bacteria may remain localized and multiply at the point of entrance, or be rapidly disseminated through the body and produce lesions at distant points from the place of entrance.

Period of Incubation.—After the introduction of the germ of an infectious disease into an animal organism a variable time elapses before the advent of the symptoms of the disease. This period is termed the period of incubation, and is fairly constant for each particular disease.

Sources of Infection

Dust is a frequent source of infection. The bacteria of tuberculosis, anthrax, influenza, and the acute infectious diseases may attach themselves to dust particles and be wafted about.

Air.—Pure air of the mountain-tops and mid-ocean is free from germs. Air is, therefore, a source of infection just in proportion to the amount of dust, carbon, and other solid particles floating in it.

Water contaminated with sewage is a frequent source of infection, especially of typhoid, cholera, and dysentery.

Milk is an excellent culture-medium in itself, and is a source of infection in typhoid fever, scarlet fever, diphtheria, and probably tuberculosis, especially in infants. Hence the necessity of rigid medical inspec-

tion and supervision of dairies, milk depots, and other sources of milk and cream supply.

Food.—Uncooked foods may carry infection. Raw oysters, which are sometimes fattened on sewage, are a prolific source of typhoid infection. Celery, lettuce, radishes, and fruits are occasional sources of infection, especially if exposed to dust and flies.

Flies, because of their pernicious habit of alighting upon and feeding upon all manner of filth and discharges, are a most formidable source of infection of all kinds, and especially of typhoid fever. Cholera, diphtheria, tuberculosis, scarlet fever, and other infections may frequently be traced to flies.

Fleas, *bed-bugs*, and *ticks* are less frequent sources of infection. The flea transmitting bubonic plague from rats to rats and from rats to man, while the tick is the source of infection of a disease peculiar to certain mountainous districts of Montana, Wyoming, and Idaho, called spotted fever. It is also the cause of Texas fever in cattle.

Dogs and Cats.—These, as well as tame rabbits, guinea-pigs, and other domestic pets, may carry disease germs on their coats or feet.

Rats, Mice, and Squirrels.—Rats are the great source of infection in bubonic plague, having the disease themselves and scattering it broadcast by means of the fleas with which they are infested. Ground squirrels have recently been found to be susceptible to plague, and

are becoming a very serious menace to certain Pacific-coast states.

Soil.—Bacteria most frequently found in soil are the Staphylococcus aureus, bacillus of tetanus, bacillus of malignant edema, and anthrax. The most important, from a surgical standpoint, being the tetanus germ.

CHAPTER VI

PYOGENIC BACTERIA, PYEMIA, SAPREMIA, SEPTICEMIA, INFECTIOUS DISEASES

Pyogenic Bacteria

While almost any germ may produce suppuration under certain conditions, there are certain forms which are particularly prone to cause pus formation. These are termed pyogenic bacteria. The more important pyogenic bacteria are the following:

Staphylococcus Pyogenes Aureus (the Golden-yellow Coccus).—This is a facultative anaërobic germ, found in soil, dust, water, the alimentary canal, on and in the superficial layers of the skin, especially of the axilla and perineum. It is the cause of 75 per cent. of acute abscesses, as boils, felons, etc. It is also the cause of certain forms of osteomyelitis and of pyemia.

Staphylococcus Pyogenes Albus (White Coccus).—A staphylococcus more feeble in power than the yellow coccus. A variety of the white coccus, called the Staphylococcus epidermidis albus, found constantly on the skin and in its deep layers, is the usual cause of stitch abscess.

Other staphylococci are the Pyogenes citreus, the lemon-yellow coccus, Staphylococcus cereus flavus and cereus albus, and Staphylococcus flavescens, all of which are of feeble pyogenic power.

Streptococcus Pyogenes.—A facultative anaërobic bacterium found in the nasal passages, vagina, and urethra. It is a much more dangerous germ than the staphylococcus and is the cause of spreading inflammations, cellulitis, puerperal fever, erysipelas, otitis media, mastoiditis, septicemia, and pyemia.

Bacillus Pyocyaneus (Bacillus of Green Pus).—Found in the skin, in the feces, and in pus; usually in mixed infections, in otitis media, peritonitis, appendicitis, etc.

Septicemia or Septic Infection

In ordinary suppuration the pyogenic toxins alone enter the circulation, causing the fever and other constitutional disturbances. In sapremia the ptomains of saprophytic bacteria, growing on blood-clots, stagnant secretions, etc., enter the circulation, causing disturbance, but in true septic infection both pyogenic germs and their toxins enter the circulation. Manifestly, such a condition is the most serious of the three, and the most to be feared of all surgical accidents.

Pyemia.—The condition of septicemia in which there are formed metastatic abscesses from septic material in the circulation becoming implanted in various parts

of the body is termed pyemia. Pyemia is, therefore, only a form of septicemia.

Mixed Infection.—In any pus infection we are apt to have a mixed infection, with several pyogenic germs, rather than a pure culture of any one germ, one germ seeming to pave the way or prepare the field for the growth of another. Thus the staphylococcus and streptococcus are frequently found in the same pus foci, while the lesions of tuberculosis and of pneumonia are frequently infected with pus cocci.

Infectious Diseases.—A list is herewith given of the more important diseases of man caused by bacteria. No mention can be made, in the space at our disposal, of the infectious diseases of the lower animals:

Tuberculosis.	Septicemia.
Influenza.	Pyemia.
Pneumonia.	Gonorrhea.
Diphtheria.	Malta fever.
Cholera.	Leprosy.
Bubonic plague.	Cerebrospinal meningitis.
Tetanus.	Syphilis.
Typhoid fever.	Relapsing fever.
Glanders.	Whooping-cough.
Anthrax.	

Malaria, yellow fever, and amebic dysentery are caused by minute animal organisms called protozoa.

Mumps, measles, scarlet fever, small-pox, chicken-pox, rheumatism, beriberi, pellagra, and infantile paralysis will all be added some day to the list of diseases whose specific germ is known. Indeed, so rapid is the advance along these lines that a list which may be considered complete to-day may be far from so to-morrow.

CHAPTER VII

PATHOGENIC BACTERIA AND DISEASES CAUSED BY THEM

MICROCOCCI

Micrococcus Lanceolatus (Micrococcus Pneumoniæ, Diplococcus Pneumoniæ, Pneumococcus of Fränkel).—A non-motile, non-spore-forming coccus, occurring in pairs. It is the cause of lobar pneumonia, also of otitis media, ulcer of the cornea, endocarditis, mastoiditis, and meningitis. It is found in the mouths of healthy individuals, though it seems not to be virulent under such conditions. It is found in great numbers in the sputum of lobar pneumonia and in the lungs, where it produces its characteristic lesions of inflammation—consolidation accompanied by high temperature. Susceptibility to infection is increased by lowered vitality from whatever cause, as age, exposure to cold and wet, other diseases, as influenza and tuberculosis, or application of other irritants to the respiratory mucosa.

Serum treatment has proved ineffectual. Sputum and excretions should be disinfected, as should the room of the pneumonia patient. There is great danger not only of others contracting the disease, but of wound

infection and mixed infection of other suppurative conditions.

Diplococcus Intracellularis Meningitidis.—The cause of cerebrospinal meningitis.

Source of Infection.—Doubtless patients having the disease, dust, and air. The avenue of infection is probably the mucous membrane of the nasopharynx. It is found in the cerebrospinal fluid, and the lesions are purulent inflammation of the pia and arachnoid, membranes of the brain, and spinal cord. High temperature, convulsions, and death in 80 to 90 per cent. of the cases, with permanent paralysis of various functions in those who recover. Prevention of infection includes disinfection of various discharges, fumigation of rooms, and cleanliness of nasopharynx.

Serum Treatment.—Flexner, working in the Rockefeller Institute, has recently perfected a serum which is curative in a large proportion of cases. Its use has already reduced the mortality of cases from 80 to 90 per cent. to about 25 per cent., and it is highly probable that its early use and more perfect technic will give a still greater reduction of mortality.

Micrococcus Melitensis.—A non-motile coccus, the cause of Malta or Mediterranean fever, a disease occurring on the Island of Malta, along the Mediterranean, in Porto Rico, the Philippine Islands, and India.

Source of Infection.—In a large percentage of the cases goats' milk has been found to be the source of in-

fection. The germs are found in large numbers in the spleen of infected animals. In man it causes a chronic remittent fever, with pains in the joints and profuse sweating. The agglutination test is positive and is used as a means of diagnosis.

Micrococcus Gonorrhœæ (Gonococcus of Neisser).—A flattened coccus occurring in pairs.

Source of Infection.—Gonorrheal pus. It is usually acquired through sexual intercourse, though contact with the pus in any manner will infect mucous membrane. It causes purulent inflammation of the urethra, vagina, uterine adenexa, conjunctivitis, ophthalmia neonatorum, or conjunctivitis of the newborn. Here the germ comes in contact with the eyes of the child during its descent through the birth-canal, which is the seat of gonorrhea.

It is also the cause of arthritis or gonorrheal rheumatism and endocarditis; 30 per cent. of the blindness in the United States is considered to be due to this cause.

Preventive measures include disinfection of discharges and hands. Sexual abstinance. In the newborn, where gonorrhea of the mother is suspected, Credé's method should be employed. This consists of the instillation of 2 per cent. solution of silver nitrate immediately, neutralized with salt solution. Protargol may be used in place of the silver nitrate. Opsonic therapy has recently been used with success in the treatment of this disorder, and vaccines are now on the market.

BACILLI

Bacillus Tuberculosis.—The discovery of the tubercle bacillus by Koch in 1882 may almost be said to mark an epoch in the history of medicine. It is a slender rod-shaped anaërobic germ found in the sputum, pus, and tissues of tuberculous lesions. It is pathogenic to man, apes, cows, sheep, horses, rabbits, guinea-pigs, and field mice. Goats and dogs are immune.

Infection occurs through the nasopharynx, lungs, and gastro-intestinal canal. Particles of dried sputum may be inhaled and infection take place in the lungs, the most frequent location of the trouble, or they may be ingested with the food, and infection take place through the tonsils or neighboring lymph-glands, or through the intestinal mucosa, especially in infants.

Entering the blood through the intestinal mucosa, they may become located in most any of the organs of the body. The most frequent locations being the lungs, lymph-nodes, bones, intestines, skin, meninges, peritoneum and pleura, testicles, ovaries, kidneys. Milk is, no doubt, a frequent source of infection, becoming contaminated in handling. At present there is some question of the transmissibility of bovine tuberculosis to humans, Koch having claimed it to be a negligible factor, while others look upon it as a frequent source of infection, especially in children. Cattle may be infected with the human variety, but it is manifestly impossible

to reverse the experiment and inoculate human beings with the bovine variety.

Pigs, monkeys, rabbits, and most other animals are susceptible to the bovine variety, and it seems unlikely that man alone should be exempt. Local infections of the skin with the bovine variety have occurred in butchers, but the infection has differed in its manifestations from similar infections with the human type. The case has not been proved, however, and until more definite data is at hand, every precaution should be taken to prevent infection with the bovine type of the disease.

The source of bovine infection, if it does occur, is not direct from the udder to the milk, except in rare instances of tuberculosis of the udder, but indirectly, by way of the intestinal canal. The most frequent seat of the disease in cows, as in man, is in the lungs. The cow does not expectorate the material coughed up, but swallows it. The feces are, therefore, teeming with the germs in an infected cow. Unless great care is exercised in stabling and milking, the milk is easily contaminated with the feces, which may be found in the dust and air of the stable.

The sputum of tuberculous patients should be received in paper sputum cups and destroyed by burning. All discharges from tuberculous foci should be destroyed. Fresh air and sunlight are detrimental to the growth and development of the germ and should be courted accordingly. Out-door sleeping and living, winter and

summer, are the most important measures with which to combat the disease, and likewise to prevent infection.

Tuberculin was formerly extolled as a curative measure, but disastrous results in many cases caused its abandonment. A new form of the preparation is again being used with success in properly selected cases. Its most important use, however, is as a diagnostic measure. Injection of it into a subject having the disease gives rise to elevation of temperature. This is called a positive reaction.

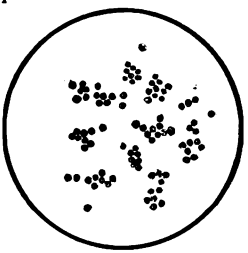
Calmette's reaction consists in placing a small amount of tuberculin on the conjunctiva. In a few hours, if tuberculosis be present, a more or less decided reaction or congestion occurs. Tuberculosis has been called the great white plague; 1 person in every 10 dies of it.

Recent statistics of postmortem examinations made abroad show that 90 per cent. of adult bodies contained either active or healed foci of tuberculosis. The Germans have a saying to the effect that "Everybody has a little tuberculosis." All of which goes to show how widespread is the disease and how curable, as many healed lesions of tuberculosis are found in people who have lived and died unconscious of having had the disease.

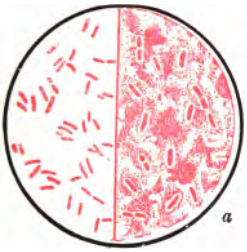
Bacillus Diphtheriæ (Klebs-Löffler Bacillus).—A non-motile, non-spore-forming, dumbbell-shaped bacillus. The germ is widely distributed. It is found in healthy throats and in the throats of those who have had the

PLATE II

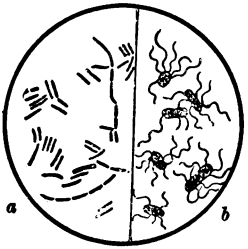
Streptococcus pyogenes (×700).



Micrococcus pyogenes aureus (× 1000).

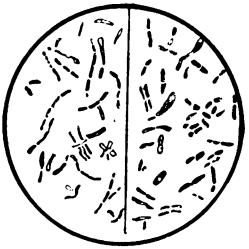


Bacillus pneumoniæ, (× 800); *a*, as seen in sputum.

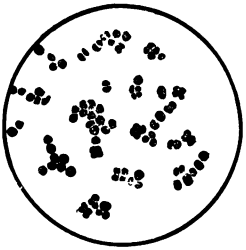


Bacillus typhosus, *a*, ordinary form (× 1000); *b*, flagellate form (× 1500).

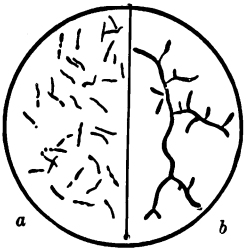
Bacillus influenzæ in nasal secretion, (× 1000).



Bacillus diphtheriæ, (× 1000).



Micrococcus meningitidis cerebrospinalis, (× 1000).



Bacillus tuberculosis; *a*, (×1000); *b*, ramified or branching form.

(Lehmann and Neumann.)

disease for months after recovery. The usual site of infection is the mucous membrane of the throat and naso-pharynx, though wounds in any location may be infected.

The germ gains entrance through some alteration of the mucous membrane and proceeds to produce its characteristic lesion, namely, a fibrinous membrane, which rapidly spreads over the contiguous mucous membrane. The germs do not enter the body, but remain localized at the site of infection. Their toxins, however, are absorbed, causing temperature, exhaustion, and occasionally paralysis of certain muscles, as those of the palate, vocal cords, and heart.

Bacteriologic Diagnosis.—Boards of health furnish an outfit containing two test-tubes. In one is a sterile swab and in the other blood-serum. A piece of the membrane or some of the secretion from the throat is obtained on the swab and smeared over the blood-serum in the tube, which is stoppered and sent to the laboratory where it is placed in the incubator for twelve hours, when, if the case be diphtheria, the germ may be recognized by examination of the culture with the microscope.

It is difficult to differentiate a diphtheritic infection from a simple tonsillitis or other angina at an early stage except by this means. As the success of antitoxin, which is the only treatment relied upon at this time, depends upon its early administration, this means of diagnosis is important. When the infection is located

in or extends into the larynx, the condition is called membranous croup or laryngeal diphtheria. The membrane may close the larynx and death from suffocation result unless intubation or tracheotomy is performed.

Prevention of Infection.—An absolutely certain preventive of infection is an immunizing dose of antitoxin. An injection of from 1000 to 3000 units is considered sufficient for immunization, while curative doses range from 3000 to 20,000 units, depending on the severity of the case and the stage at which the antitoxin is administered.

A rare and curious condition exists in some individuals, in which the person is said to be sensitized to horse-serum. In such persons, who are frequently asthmatics, the administration of antitoxin may give rise to severe asthmatic paroxysms, cardiac weakness, suspension of respiration, and even death. It is a remarkable thing that most of such people are frequently thrown into asthmatic paroxysms by the presence of a horse or the odors of horses.

Bacillus Typhosus (Bacillus of Eberth).—A [redacted]-motile, facultative anaërobic bacterium. There is practically but one source of infection, the feces or urine of a typhoid patient, and one avenue of infection, the digestive tract, so that to have typhoid fever one must virtually eat some one's excreta, no matter with what dish it may be served. A contaminated water-supply is the greatest agent of infection.

Next to water, milk is the most frequent carrier of the infective germ. Raw oysters and uncooked vegetables may convey the infection. The pernicious practice of fattening oysters on sewage has been the cause of untold deaths of typhoid fever in the past. Flies frequently carry the infection from out-houses to foods of various kinds. The site of infection is the Peyer's patches of the small intestine, though the germ is found in the blood, milk, spleen, liver, and lymphatic glands, and it is thought it may gain entrance through the tonsils. Locally, there may be ulceration of the intestines, which ofttimes leads to hemorrhage and even perforation. The symptoms of the disease are those of a continued toxemia, fever, exhaustion, and delirium.

Typhoid Carriers.—Cultures of bacteria may remain in the gall-bladder or other organs for months or even years, the individual suffering no inconvenience, and thus becoming a walking source of infection for others.

Widal Test.—When the blood of a person suffering from typhoid fever is mixed with a living culture of typhoid bacteria and examined in the hanging drop with the microscope, the bacteria are seen to clump together and cease their movements. This is due to the agglutinating property of the blood in this infection, spoken of elsewhere.

Drying of the blood and considerable dilution does not interfere with its accuracy, so that in practice a drop of blood is drawn on to a piece of filter-paper and sent to

the laboratory, where it is soaked out with water and added to the culture.

Prevention of Infection.—A vaccine has been prepared from dead cultures of the bacillus which raises the opsonic index for this germ, and gives so high a degree of immunity that it is coming into universal use.

The best means of combating the spread of the infection is absolute sterilization of all excreta from typhoid patients by thoroughly mixing with formaldehyd and allowing to stand for several hours, stirring in the meantime. Pure water- and milk-supply or sterilization of same. Extermination of flies and vaccination.

CHAPTER VIII

PATHOGENIC BACTERIA AND DISEASES CAUSED BY THEM (Continued)

Bacillus of Tetanus.—A slightly motile, spore-forming anaërobic bacterium.

Sources of Infection.—The germ is widely distributed, occurring in garden earth and the feces of herbivorous animals.

The avenue of infection is practically always a wound, and usually, because of the anaërobic nature of the germ, a punctured wound. Fourth of July injuries, in which pieces of wad and paper are blown into the hand, are prolific sources of tetanus infection.

Lesions.—The site of infection causes but little trouble, as this is an example of a purely toxic disease. The toxin, which is very virulent, is absorbed and acts upon the cells of the central nervous system in a manner resembling strychnin, causing convulsions and opisthotonos. To stand helplessly by and watch the agonizing struggles and convulsions of a patient afflicted with tetanus, and listen to his pleading for relief, is one of the most heart-rending experiences a nurse may be called upon to endure.

Antitoxin.—An antitoxin is prepared from the horse in the usual manner, but to be of value it must be given

very early indeed, as the fatal dose of the toxin is so infinitesimal. Its greatest value is as a prophylactic measure in cases of suspected infection. If given at the time of infection it is an absolute preventive.

Preventive measures include the exposure to air of all punctured wounds, opening them to admit air to all parts, and the immediate injection of antitoxin in all cases of suspected infection, as blank-cartridge wounds, nail wounds, and all punctured wounds caused by blunt instruments that are contaminated with soil or manure.

Bacillus of Influenza (Bacillus of Pfeiffer).—A non-spore-forming, non-motile aërobic bacterium found in the sputum, bronchial and nasal secretions of those suffering from the disease. It has never been discovered outside the body, and probably is always transmitted from patient to patient. It produces catarrhal inflammation of the respiratory mucous membranes with constitutional symptoms of fever, depression, exhaustion, etc., indicating the presence of a toxin, though it has not yet been demonstrated.

Bacillus Anthracis.—A non-motile, aërobic, spore-forming bacterium. Its spores are the most resistant of any known germ, having been known to withstand boiling for half an hour, 5 per cent. carbolic acid solution for forty days, and 1:1000 bichlorid solution for three days. Because of this great resistance it is used as a standard for determining the potency of various germicides and antiseptics.

It is the cause of anthrax, a disease more particularly of cattle and sheep, man only acquiring it from contact with these animals or their products. Woolsorters' disease is anthrax of the lungs in man. It occurs in those who handle wool from sheep which have been affected. Infection usually occurs through wounds of the skin, where it produces a localized inflammation termed malignant pustule.

Animals are rendered immune to disease by vaccination with attenuated cultures of the germ. There is some risk attached to this method, and it is never employed in man.

Bacillus Mallei (Bacillus of Glanders).—A facultative anaërobic, non-spore-forming bacterium, the cause of glanders. Like anthrax, glanders is a disease of the lower animals more particularly, man acquiring it by contact with such animals.

The *source of infection* is the discharge from the lesions of the disease, and the *site of infection* is the nasal mucous membrane or wounds of the skin. Nodules of the skin and mucous membranes occur and break down, forming ulcers. The neighboring lymph-glands become swollen and a profuse discharge occurs, which is highly infective.

Mallein, a product similar to tuberculin, is used as a diagnostic measure in animals. A reaction similar to that following the use of tuberculin follows its use in affected animals. Prevention consists of prompt kill-

ing of affected animals, and proper disinfection of their quarters.

Bacillus Lepræ (Bacillus of Leprosy).—A non-motile bacillus. Spores have not as yet been demonstrated. Sources of infection have not yet been determined. Lesions are thickening and nodules of granulation tissue in the skin and peripheral nerves, though other tissues and the internal organs may be affected. It is uncertain whether the disease may be transmitted from one person to another or not.

Leprolin.—This is a substance analogous to tuberculin, and is prepared from cultures of lepra bacilli. It is used as a diagnostic measure and has shown little or no curative properties.

Bacillus of Bubonic Plague.—A facultative anaërobic, non-motile, non-spore-forming bacillus, the cause of bubonic plague.

Source of Infection.—Fleas carry the infection from rats to man and other animals, particularly ground squirrels. Direct infection from dust or air seldom if ever occurs. Infection doubtless always occurs through the skin by the bite of a flea or fly, usually the rat flea.

No local reaction occurs at the site of infection, but inflammation of the neighboring lymphatic glands soon follows.

Three forms of the disease are recognized: bubonic, distinguished by enlargement and suppuration of the

lymphatic gland (buboes); pulmonic, where the lungs bear the brunt of the attack; septicemic, a generalized form of the disease.

Preventive Measures.—Destruction of rats and their fleas. The rat flea normally does not attack man, but when the rats die and become cold the fleas leave the bodies and seek warmth and nourishment wherever they may be found. It is thus that they are forced to seek sustenance upon an abnormal host.

Vaccines have been used with some success in establishing immunity to the disease; an antitoxin is also being used with encouraging results in the treatment.

SPIRILLA

Spirillum Choleræ Asiaticæ (Comma Bacillus of Cholera).—An aërobic, motile, non-spore-forming bacterium of the spirilla class. It is the cause of Asiatic cholera, one of the most dreaded diseases of ancient and modern times.

The *source of infection* is usually drinking-water; less frequently, food or other ingested material.

The *avenue of infection* is always the intestinal canal. Like typhoid fever, cholera is always a filth disease. To be infected one must always swallow the excreta of some one having the disease. Flies act as carriers, as in typhoid.

Lesions are localized in the intestinal canal and the spirilla are not found in the blood. It is essentially a

toxic disease, as injection of the toxins produce typic symptoms of the disease.

Symptoms are diarrhea, fever, prostration, and clammy skin, etc.

The agglutination test, as in typhoid, is positive.

Protective vaccines have been used with considerable success, but efforts to produce an antitoxin have been unsuccessful.

Treponema Pallidum (Spironema Pallida).—A minute spiral-shaped motile organism, found in chancre, lymphatic glands, and in secondary lesions, mucous patches, ulcers, and all organs in hereditary syphilis.

The *source of infection* is the discharge from the primary lesion or chancre, the secondary lesions, or suppurative lesions of the tertiary stage. The organism evidently enters the blood at once, as removal of the chancre or site of primary infection at the earliest possible moment fails to prevent the disease.

Means of infection is usually through sexual intercourse by introduction of the germ through minute abrasions of the skin or mucous membrane of the genital organs. It is acquired innocently, especially by nurses and physicians, or any one coming in contact with the discharges of syphilitic sores.

Prevention consists in avoidance of such sources of infections, both sexually and otherwise, and strict antiseptic precautions or rubber gloves in handling syphilitic patients. The only animal known to be susceptible

to syphilis is the anthropoid ape, so that infection is always from individual to individual or is inherited, that is, from mother to child, or father to child.

Spirillum of Relapsing Fever.—A motile spirillum with flagella, the cause of a recurrent or intermittent fever. It is found in the blood of patients suffering from the disease, but only during the period of fever. After the attack the spirilla congregate in the spleen and finally die there.

The agglutination test is positive. The germ is pathogenic to man and monkeys, and is transmitted by the bite of the bed-bug.

CHAPTER IX

PROTOZOA AND DISEASES CAUSED BY PROTOZOA

Plasmodium Malariæ.—There are three species of this parasite, each giving rise to a different type of malarial fever:

The *tertian variety*, in which the parasite reaches maturity in forty-eight hours, and causes the benign tertian type of the disease.

The *quartan variety*, which reaches maturity in seventy-two hours, and causes the benign quartan type of the disease.

The *estivo-autumnal variety*, developing to maturity in twenty-four to forty-eight hours, and causing the malignant estivo-autumnal type of the disease.

The *source of infection* is the bite of the mosquito, in whom the sexual cycle of development of the parasite occurs. The mosquito can only become infected by sucking the blood of a malarial patient.

Amœba Dysenteriæ.—A protozoön the cause of amebic dysentery. Found in the intestinal ulcers, feces, and secondary liver abscesses of those suffering from the disease. Source of infection is unknown.

Trypanosomata.—Trypanosomes are flagellated motile protozoa. Various varieties occur, causing numerous diseases of animals. One variety causes the peculiar sleeping-sickness of Africa, the tsetse-fly being the means of infection.

CHAPTER X

ANTISEPTICS, DISINFECTANTS, AND GERMICIDES

Germicide.—An agent capable of killing bacteria.

Disinfectant.—Also an agent capable of killing bacteria. The term, however, is usually restricted to such germicides as are used to disinfect rooms, buildings, cars, and similar structures.

Antiseptic.—A substance capable of preventing the growth and development of germs, but not necessarily destroying them. A disinfectant or germicide is necessarily an antiseptic, but an antiseptic is neither a germicide nor disinfectant. A disinfectant is the term used in speaking of a germicide used for destroying the contagion after contagious disease, to disinfect discharges, excreta, clothing in infectious diseases, and to prepare the hands, the field of operation, and room in which an operation is to be performed. An antiseptic is used for the purpose of keeping wound dressings aseptic, or to assist nature in conquering infection after it has occurred. Most disinfectants or germicides in germicidal strength are too strong for use in wounds, as they may destroy the tissue cells as well as the bacteria.

Deodorants are substances which destroy odors. While germicides may do this, the term is usually re-

stricted to substances which without germicidal action simply disguise or destroy odors.

Sterilization is the destruction of bacteria and their spores by heat or other means.

Heat.—Where applicable, heat is the most efficient disinfectant we have. There are, however, many things which cannot be subjected to boiling, high dry heat, or the open flame.

Steam is the most general means of employing heat. Surgical dressings, cotton, gauze, bandages, gowns, caps, face-masks, etc., are best sterilized by means of steam in a properly constructed apparatus or sterilizer.

Superheated steam (*i. e.*, steam under pressure) is more efficient and more rapid in action, but the ordinary sterilizer does not take advantage of this principle, and more time must, therefore, be allowed than in the pressure apparatus. One hour is considered sufficient for the sterilization of ordinary dressings, gowns, etc., with the low-pressure sterilizer, while half that time is sufficient with the high-pressure apparatus.

Disinfectants and Antiseptics

Mercuric Chlorid.—Bichlorid of mercury is a corrosive poison, usually supplied in tablets which are colored blue. It is probably the most used of all germicides. It is used in solutions of 1:1000 to 1:5000 strength. Its most useful field is in the disinfection of hands, the site of operation, and elsewhere on the unbroken skin.

Because of its toxic properties it is unsafe for use in irrigation of cavities, and because of its irritating and corrosive action unsuited for wound dressing. By coagulating the albumin of the wound discharges it defeats its purpose as an antiseptic and is extremely painful besides.

Mercuric Iodid.—This is a germicide of much power, and because of its not coagulating albumin is of greater value in some conditions than the bichlorid. It is combined with potassium in the form of a soap, which makes an ideal hand disinfectant.

Silver Nitrate.—This is a caustic poison of high germicidal value, but owing to the unstable property of its solutions, the silver being precipitated by chlorids or inorganic salts, it is of little clinical value. Its most important use is in Credé's method for the prevention of gonorrheal infection of the eyes of the newborn, where a 2 per cent. solution is instilled into the eyes and immediately neutralized with normal salt solution.

Carbolic Acid.—A poison of high germicidal value extensively used, especially in domestic practice. It is used in from 1 to 5 per cent. solution, and finds its greatest field of usefulness as an all-round antiseptic in the treatment of infected wounds.

Gangrene of the fingers and toes has followed its prolonged use as a wet dressing. Caution should, therefore, be used in its application on dressings, bandages, etc.

Lysol.—This is a coal-tar product closely related to carbolic acid, but far less poisonous. It is largely supplanting the latter for hand disinfection and in obstetric practice. It is used in 1 to 5 per cent. solution.

Iodin.—This is one of the most efficient germicides we possess. In the form of the tincture it is used to cauterize corneal ulcers and as an application to indolent ulcers and suppurating surfaces. A 1: 1000 solution in water is used for hand disinfection. It has the disadvantage of staining the hands, which must be decolorized with solution of ammonia. It is coming into frequent use on the Continent for preparing the field of operation, the skin being simply swabbed with the tincture and all scrubbing dispensed with.

Its greatest use is in the preparation of catgut ligatures, which it not only renders sterile, but antiseptic, thus tending to prevent stitch abscess.

Potassium Permanganate.—This is a germicide formerly much used in hand disinfection. It stains the skin a mahogany brown, and it is necessary to follow its use with a solution of oxalic acid to remove the stain. Its use now is restricted mostly to the treatment of gonorrhea.

Formalin is a 40 per cent. solution of formaldehyd gas. It is a powerful germicide, and owing to its gaseous nature is the best disinfectant we possess for fumigating rooms, dwellings, cars, etc., after contagious dis-

ease. It is harmless to colors, metals, clothing, etc., but because of its highly irritating character it is practically useless for purposes where it would come in contact with the human tissues, as in hand disinfection, wound dressing, etc. It is used to sterilize eye and ear instruments whose delicate edges forbid their being boiled. The formalin is vaporized in a closed space where the instruments are placed. For fumigating rooms after contagious diseases the vaporization of the formaldehyd gas is accomplished by adding to the formalin potassium permanganate in the proportion of 8 ounces of potassium permanganate to 16 ounces of formalin for each 1000 cubic feet to be fumigated.

When the two drugs are mixed a rapid effervescence takes place, with the production of considerable heat, whereby the gas is vaporized. The vessel containing the mixture should be placed within another containing water, as the heat may be sufficient to ignite wood or other inflammable substances with which it comes in contact. Bedding, clothing, etc., should be spread out, and drawers and boxes opened to allow the gas to gain access to them. All doors, windows, or other openings should be closed and paper or adhesive plaster pasted over all cracks or crevices where the gas might escape. The gas should be allowed to remain in the room for at least ten hours.

Acetozone.—This is a new non-poisonous germicide of great value. It is of value only in solutions, and as

such solutions are very unstable they must be prepared as needed. It is used in solutions of 1: 1000, and because of its non-toxic character may be used with impunity about the nose, mouth, and throat, where more poisonous germicides may not be used. It is used internally as an intestinal antiseptic, but owing to its unstable character it is doubtful if it ever passes the stomach and reaches the intestines in its original form. It may be used with satisfaction for colonic flushing in dysentery and colitis.

Turpentine.—This is a germicide of some value, but of limited use. The late Nicholas Senn was wont to resort to its use very frequently, especially before operations that involved the opening of the synovial sacs of joints. Its addition to the ordinary green soap used in hand disinfection materially increases the usefulness of the latter.

Alcohol is a disinfectant used principally in hand disinfection, where, because of its solvent action on the fatty matter of the skin, it is of peculiar value. It thus brings the germs out of the pores to the surface, where they may be destroyed by it and other germicides. It is also much used for the preservation of pathologic specimens.

Hydrogen Peroxid.—This is a liquid which depends upon the oxygen in its composition for its antiseptic virtue. It is not of great antiseptic value, but owing to its property of decomposing pus it is much used for

cleansing suppurating wounds and loosening dressings which have become adherent from dried secretions. It should never be used in suppurating cavities where there is not a free outlet for the gas which is formed by its decomposition, as the pressure might force septic material out into healthy tissue.

Iodoform.—This is a yellow powder of high iodin content. It was formerly much used as an antiseptic in dry dressings. It is in itself not antiseptic, and should be sterilized before use on a sterile wound, but in contact with pus it is decomposed, giving off free iodin, which in turn acts as an antiseptic. Because of its particularly obnoxious odor and slight germicidal value it is rapidly falling into disuse.

Aristol (Thymol Iodid).—This is a reddish-brown powder containing 45 per cent. iodin. It has almost supplanted iodoform as a dry dressing, being free from its disagreeable odor and less toxic.

Formidin.—This is a reddish powder containing formaldehyd, salicylic acid, and iodin in combination. It is of greater value than either of the last-named drugs. Being non-irritant and practically non-toxic, it may be used both internally and externally without danger. In the presence of wound secretions, pus, or the intestinal secretions it breaks up into its component parts—iodin, formaldehyd, and salicylic acid—all of which are antiseptics. It is used as a dressing powder and for the preparation of antiseptic gauze.

Bismuth Subnitrate.—This is a white powder of very little antiseptic value. It has recently sprung into prominence for the treatment of tuberculous cavities of bone and suppurating disease of the accessory sinuses of the nose. It is used in the form of a paste combined with bismuth, iodid, and petrolatum.

CHAPTER XI

SUSCEPTIBILITY AND INFECTION

SUSCEPTIBILITY, as we have learned, is that condition of the animal organism which permits of the growth and development in its tissues of a disease germ with the production of the characteristic symptoms and lesions of the disease of which it is the cause.

It is the opposite of immunity. Varying conditions and circumstances produce varying degrees of susceptibility. No germ is capable of producing disease in all animals under all conditions.

Age is often an element in susceptibility, the young of all animals being generally more susceptible to infection than the adult. The increased susceptibility of children to measles, scarlet fever, and whooping-cough is well known. Certain germs are capable of producing disease in some animals and incapable of producing it in others. Frequently the susceptibility of the host depends upon the virulence of the germ. Likewise, the severity of the disturbance produced depends largely upon the virulence of the infecting germ, as well as upon the resistance or susceptibility of the host. Again, the degree of susceptibility depends upon the number of germs which

gain entrance into the body of the host. A few virulent germs may succeed in establishing an infection where a larger number of attenuated ones might fail.

The route by which the germ gains entrance to the body has also an influence upon the susceptibility of the animal to infection, intravenous injection of germs producing infection where subcutaneous injections fail. Certain germs have certain routes of entrance to the body, and entrance by any other route reduces the chances of infection or reduces the intensity of the process when infection occurs. The resistance to cholera infection is greater in subcutaneous infection than when infection occurs by way of the intestinal canal, the usual route. Lowered vitality from an attack of one disease often increases the susceptibility to another infection, as in the susceptibility to tuberculosis following measles.

Fatigue is, without doubt, responsible for a great deal of increased susceptibility. White rats, which are immune to anthrax, become susceptible when fatigued. Starvation also reduces the resistance. Pigeons, which are immune to anthrax, become susceptible upon starving. Heat, cold, and moisture also increase the chance of infection, as was shown by Pasteur, who, by immersing a hen in water, made her susceptible to anthrax, to which chickens are normally immune. Improper food and drugs may increase the chances of infection. Hankin fed immune rats on sour milk and bread and made

them susceptible. Inhalation of ether increases the susceptibility to pneumococcic infection.

Injury and perverted function also increase the susceptibility to infection. Thus, tuberculosis of the joints and bones frequently follows traumatic injury, while diminution of the acidity of the gastric juice increases the susceptibility to cholera infection. Infection coincidently of saprophytic germs with tetanus bacillus increases the chances of tetanus infection.

In some infections, as pneumonia, the susceptibility is increased by a previous attack of the disease, while in others immunity is conferred by an attack, as in smallpox, or decreased susceptibility occurs without producing complete immunity, as in diphtheria.

The coverings of the external surface of the organism, the skin, and mucous membranes present certain obstacles to infection. Many conditions arise to destroy the integrity of these coverings and thus increases the susceptibility to infection.

The unbroken skin is practically impervious to germs, though they doubtless do obtain entrance occasionally by way of the hair-follicles and the ducts of the sweat-glands. Scratches, minute abrasions, and other breaches of continuity let down the bars for the entrance of germs, though they are often destroyed by phagocytosis immediately upon their entrance.

The mucous membranes of the mouth, throat, and nasal cavities normally present considerable resistance

to infection, as is shown by the frequent presence upon them of virulent germs, as the diphtheria and influenza bacillus and the streptococcus in persons in perfect health. The constant flow of mucus and the movement of the ciliated epithelium tend to prevent the entrance of the germs through these surfaces, but injury, excessive drying of the surfaces from overheated rooms, and disease may lower the resistance offered by these surfaces and increase the liability to infection.

Few bacteria reach the lungs, but those that do are quickly taken up by the fixed epithelial cells and the leukocytes. Under certain unfavorable conditions this does not occur, and infection occurs through the lungs. The stomach is exceptionally free from infection. This is doubtless due to the fact that the gastric juice is detrimental to bacterial activity. It is not germicidal, however, and therefore does not prevent the entrance into the intestines of bacteria, which may there cause trouble.

The intestines present a feeble resistance to bacterial activity in the bile, but, on the whole, bacteria do fairly well in the intestinal contents. The intestinal walls normally, however, present considerable resistance to the entrance of germs, as is evidenced by the large number of bacteria found in the intestinal contents of healthy individuals, even typhoid bacilli and cholera germs having been found in the bowel movements of healthy persons. Certain conditions, as improper feeding,

heat, depression, and other unknown influences, increase the susceptibility to intestinal infection.

Transmission of Infection

With the exception of the tetanus bacillus, which lives naturally upon the soil and the intestinal contents of horses, most pathogenic bacteria can exist but a short time outside the animal body. Transmission of infection usually occurs by direct contact with an individual having the disease or with a secretion from his body.

The gonococcus dies very soon outside the body, the pneumococcus is longer lived, and the typhoid bacillus and tubercle bacillus can exist for a considerable length of time outside the body. The diphtheria bacillus and typhoid germ even grow and develop in milk. Not a few epidemics have been traced to this source. Recent investigations tend to show that the germ carrier is responsible for the transmission of many cases of infection.

Carriers are individuals who after recovery from disease continue to throw off virulent germs for long periods of time, or others who, after contact with infected persons, carry the germs in their nose, throat, or intestines, though themselves healthy. Among the diseases thus transmitted are typhoid fever, cholera, influenza, pneumonia, and diphtheria.

Germs which leave the body with intestinal excretions, as in typhoid and cholera, are likely to contaminate a

water-supply and thus be transmitted to others, or to contaminate the feet of flies, which, in turn, infect some food. Those which leave the individual in the exhaled air, as tubercle bacilli, pneumococcus, or diphtheria germs, are likely to be inhaled or ingested with food, or they may infect eating or drinking utensils.

Certain insects may be the means of transmitting infection. The fly may carry typhoid, cholera, tuberculosis; the flea transmits the plague; the mosquito, malaria and yellow fever; the tsetse-fly, sleeping-sickness.

Prevention of Infection

General Precautions for Nurses

The nurse in charge of a case of infectious or contagious disease owes a duty not only to the patient, but to herself, to the family, and to the public. She should use every care to protect herself from infection, that her usefulness to the patient, the family, and to the public may not be curtailed or destroyed. She should, therefore, avail herself of every protection possible before entering upon the case.

In the first place, she should be in perfect health. Any nurse who expects to nurse typhoid fever should have been vaccinated against the infection long enough before going on a case for immunity to have been established. In diphtheria she should have had an immunizing dose of antitoxin. She should be scrupulously

clean as to her hands, nails, teeth, and hair, and should not eat or drink in the sick room.

She should not lower her vitality by overwork and loss of sleep, but in difficult cases should have assistance.

Her duty to the family demands that she do everything in her power to prevent other members of the family from becoming infected, and to that end she should educate them in the dangers of infection and the precautions necessary to avoid it.

Indeed, one of the greatest values of the trained nurse lies in the educational value of her services, the example of surgical cleanliness which she exhibits, and the conception of sanitation and disease prevention which the laity gain from her.

Her duty to the public consists in preventing the spread of the infection by insisting upon the proper observance of quarantine, the rigid exclusion of flies and domestic pets, as cats and dogs, many infections being spread by these agencies. She should demand the disinfection of milk bottles or other utensils taken from the place, and in the absence of the physician or other authority she should oversee the process of disinfection and fumigation.

After leaving a case of infectious disease the nurse should, if possible, determine if her throat be free from germs, that she does not become a healthy carrier of germs. She should avoid for some time, if possible,

caring for patients who would be especially susceptible to the disease which she has been in contact with, such as children or confinement cases after scarlet fever, and surgical or obstetric cases after erysipelas or septic infections.

SPECIAL PRECAUTIONS: DISINFECTION AND FUMIGATION

In disinfection in infectious disease the method to be followed depends upon the nature and characteristics of the infecting agent and the manner in which the germ is thrown off. In cholera and typhoid fever the germ is thrown off with the urine and feces, while in pneumonia, diphtheria, and tuberculosis it is found in the sputum.

Typhoid Fever, Cholera, Yellow Fever.—Exclude flies. The feces and urine should be received in a vessel containing a 5 per cent. solution of carbolic acid or 1: 1000 solution of bichlorid of mercury. They should be allowed to stand an hour, being stirred several times before emptying. The water-closet, seat and bowl, and the bed-pan should be washed daily with carbolic or sublimate solution. All bed-linen, garments, towels, handkerchiefs worn or used by the patient should be immersed in 5 per cent. carbolic or 1: 1000 solution of bichlorid for an hour and boiled. Rubber gloves should be used while bathing a patient. All vomited matter should be disinfected in the same manner as the stools and urine.

The nurse should, if possible, have been vaccinated

against typhoid. She should disinfect the hands after handling the patient with bichlorid solution.

All dishes, trays, glasses, cups, and other eating utensils should be washed with bichlorid and boiled. All remains of liquid food should be mixed with carbolic or sublimate solution and all solids burned. All toys, books, pencils, or writing material should be disinfected before being handled by others, or burned.

The patient's hands and parts of the body that become soiled with discharges should be washed with 1:1000 bichlorid solution. These precautions should be followed until the temperature has been normal at least a week, when the room and furniture should be disinfected. All wood work, wooden furniture, iron beds, springs, etc., should be washed with 1:1000 bichlorid solution. All rugs, portières, curtains, and draperies should have been removed from the room. If they have not, those that can be boiled should be, and the rest should be placed where formaldehyd can reach them to the best advantage; the windows and doors should be sealed and formaldehyd generated either with a special apparatus or by the permanganate method, as described in an earlier chapter.

Diphtheria, Scarlet Fever, Measles.—Exclude flies. All precautions for typhoid and cholera, except disinfection of the stools and urine, should be carried out in diphtheria, scarlet fever, and measles, with additional precautions to prevent the dissemination of the germs

in the sputum and nasal secretions; and in scarlet fever and measles, in the scales. The sputum should be received in a cup or receptacle containing carbolic or sublimate solution. The patient should be taught to cough and blow the nose into a rag or handkerchief, which should be disinfected or destroyed.

In scarlet fever and measles the body should be anointed with camphorated or mentholated oil to prevent flying of the scales. A warm antiseptic bath should be given daily, followed by the oil rub until desquamation is complete. A gown and overshoes should be kept outside the door for use of doctor or others who enter the room. Upon release from quarantine, the patient should take an antiseptic bath and shampoo, leave all clothing in the room, and dress in a room which has been isolated from the sick room or has already been disinfected. The nurse should do likewise, all clothing being left in the room to be fumigated.

In diphtheria it is advisable that the nurse should have an immunizing dose of antitoxin, and wherever possible cultures should be taken from her throat after quarantine to see that she does not become a carrier. Should she harbor the germs in her throat she should not go on another case other than diphtheria until her throat is free from germs. After nursing scarlet fever a nurse should, wherever possible, refuse to nurse a confinement case or a child with another disease until some time has elapsed.

Tuberculosis, Pneumonia, and Influenza.—Exclude flies. In these diseases the sputum carries the infection; the nasal secretions also in influenza. These secretions, therefore, are the ones that require particular attention. They should be carefully guarded against dissemination by the use of sputum cups and gauze or handkerchiefs, which may be immersed immediately in disinfectant solution or burned. Dishes, eating utensils, bed-linen, garments, food, etc., should receive the same care as in typhoid and other infectious diseases. Rooms should be disinfected and fumigated as in other infections.

Small-pox.—Exclude flies. In this disease the scales constitute the most important element in the dissemination of the infection. Effort should, therefore, be directed toward eliminating, as far as possible, this source of contagion. The contagion is very persistent and clings to clothing, furniture, the skin and hair of attendants, and to everything that may come in contact with or near the patient. The room should be as bare of furnishing as possible. Every precaution should be exercised by the physician and others who must pass in and out of the building where the case is isolated. A complete outfit should be at hand to protect shoes, clothes, and hair when entering the room or building. Everyone in contact with the patient should have been vaccinated. Antiseptic baths and shampoos should be given daily for some time before release. The nurse should take similar precautions, though not so extensive. Fumigation

with formaldehyd should be carried out in the usual manner.

Cerebrospinal Meningitis and Infantile Paralysis.—Exclude flies. While the means of dissemination of these diseases are not as yet well understood, the frequent presence of the meningococcus in the secretions of the nose and pharynx, and the fact that the nasal secretions in infantile paralysis have been shown to be infectious for monkeys, are sufficient reasons for especial attention to these secretions. The laws regarding quarantine in these diseases are very lax as yet, but strict isolation should be insisted upon and every precaution taken to prevent the spread of the infection, and until more complete knowledge is available regarding these diseases, fumigation of the rooms occupied by the patient would be only the part of wisdom, as would the use of Flexner's antitoxin on nurse and attendants in meningitis.

Erysipelas and Suppurative Diseases.—Exclude flies. These, being more especially surgical infections, are of greater danger to persons having open wounds, to women in confinement, etc. The precautions necessary are less exacting. Pus, scales, crusts, and wound discharges should be carefully burned or disinfected.

If there be a possibility of the room being used for a surgical confinement case at any future time, it should be fumigated.

CHAPTER XII

IMMUNITY

The Causes and Mechanism of Immunity

Natural immunity, as we have learned, is that resistance to certain diseases possessed by certain species of animals.

It is dependent upon many different conditions and circumstances. Certain profound differences in the life processes of the different species of animals are sufficient to account for many instances of natural immunity. Thus, the immunity of cold-blooded animals to most diseases of warm-blooded species may be explained upon this ground. The tissues of the immune individuals do not present favorable soil and environment for the growth and development of the germs which cause that particular disease. Just what the conditions are which are detrimental to the activities of the germ we are not able to determine to any great extent.

True, we are able in certain cold-blooded animals to convert this immunity into susceptibility by placing the animals in a warm place. Doubtless, by subjecting the immune individual to the same environment, the same food, and the same mode of living we might be able to

influence the immunity to a greater or less extent in some instances. But it is just as probable that in some cases the immunity is dependent upon conditions so deep rooted and so unalterable as to defy environment, food, or mode of living. From which we may gather that in certain instances the natural immunity is only relative, while in others it may be looked upon as absolute. Unquestionably, many instances of natural immunity are closely related to acquired immunity in their mechanism and cause, and are dependent upon the presence in the tissues and body fluids of the several complex and highly interesting substances which are referred to collectively as antibodies and to the conditions which their presence induces. We may, therefore, consider the manifestations of acquired immunity for a better conception of the natural form of this condition.

Acquired Immunity

Acquired immunity is said to be either active or passive. Active immunity is that form of immunity in the production of which the cells of the individual take an active part. Of this character is the immunity which follows an attack of certain infectious diseases, as smallpox. So also is that produced by inoculation with an attenuated form of the disease, as in vaccination with cow-pox, and that produced by injections of dead cultures of the causative germ, *i. e.*, bacterial vaccines.

Passive immunity is defined as that form of immun-

ity in the production of which the cells of the organism take no part. It is probably always artificial, and is exemplified in the use of an immunizing dose of diphtheria antitoxin or of tetanus antitoxin. The antitoxin is introduced ready prepared into the blood of the organism, whose cells are, therefore, under no necessity of producing further antitoxin, and so take no active part in the process. Such immunity is less lasting than the active form because the antitoxin is soon eliminated, while in the active form of immunity the cells go on elaborating antitoxin and other antibodies for a considerable time after the recovery from the disease or inoculation whereby the immunizing process was brought into action.

In the study of active immunity numerous factors must be taken into consideration, all of which have a part in this complex phenomenon. Of these factors, first place is probably occupied by the phagocytes, as they are doubtless concerned in the resistance of all forms of infection. Then there are the opsonins, without which the phagocytes are helpless. The antibodies, consisting of antitoxins, bactericides (alexins, etc.), and bacteriolysins, and lastly, the agglutinins, of whose part in the process we are yet more or less in the dark.

Of these various substances and processes doubtless in certain infections one plays a leading rôle, the others being content with minor parts, while in other diseases their relative importance may be reversed, depending

upon the nature of the infection. In diphtheria, which is an example of a toxemia, antitoxin plays the leading part, while the phagocytes perform a subordinate function in destroying the germs which are producing the toxin. In suppurations, as in gonococcus or staphylococcus infections, in which the toxins are of secondary importance in the production of the diseased processes, phagocytes and bacteriolysins bear the burden of the fight. Rabbits and dogs are both relatively immune to pneumonia, but the germs develop more readily in the rabbit than in the dog. The rabbit, however, is less susceptible to the poison than the dog, which would indicate that in the rabbit the antitoxin was the basis of immunity, while in dogs who are susceptible to the toxins, but on whom the germs do not thrive, the immunity is more than likely due to the phagocytosis or the bactericidal bodies.

Briefly summarized, the part performed by the various factors in immunity are as follows: The phagocytes or white blood-corpuscles leave the blood-vessels and flock to the site of infection or the local lesion, there to devour and destroy the invading germs.

The antitoxins neutralize the toxins produced by the germs. If the toxins are excreted by the germs and taken up by the blood, as in diphtheria, it does this unaided. If, however, as in cholera, the germs themselves enter the blood and carry their poisons within their bodies, the bacteriolysins must, by dissolving the germs, set

the toxin free before it can be neutralized by the antitoxin, but before the bacteriolysins can dissolve the germs it is necessary for the bactericides or alexins to destroy them.

If these substances for a certain germ (for it should be understood that they differ for different germs) exist in sufficient quantities and the processes described are sufficiently active, immunity to that germ must exist. If these immunizing substances be not present, the introduction of the germ into the body stimulates their formation, and if recovery occurs, they remain in the body in sufficient quantities to prevent any such germ from obtaining a foothold in that territory for a varying length of time.

Whether natural immunity to toxin is due to the presence in the blood of antitoxin or to a lack of affinity between the toxin and the body cells, or to both, we are unable to say. It is a fact that in some instances antitoxin is found in the blood of healthy animals which are immune to a certain toxin. In others no such antitoxin is present, and yet immunity exists, due perhaps to a lack of affinity between the toxin and the cells of the organism. The tortoise is unaffected by injections of tetanus toxin, but if the blood of a tortoise which has been injected with tetanus toxin be injected into a susceptible animal, death results, showing that the toxin is not neutralized by the antitoxin or otherwise destroyed.

Inherited Immunity

Natural immunity is, of course, transmitted from parent to offspring, but acquired immunity is transmitted but slightly, if at all. A certain degree of immunity is transmitted by the female immunized animal to her offspring in certain instances, as in the case of sheep immunized to anthrax, but this does not obtain in case of the male parent.

A certain degree of passive immunity occurs in the newborn whose mother has had recent injections of antitoxin. Antitoxin may also be transmitted from mother to offspring through the milk. The immunity thus conferred is not sufficient to be depended upon, and further immunizing procedures should always be instituted. Agglutinins are occasionally transmitted to the offspring. Opsonins are not transmitted to the offspring in the uterus, but are present in the milk of nursing animals, and they are probably absorbed by the nursling *via* the digestive tract.

Methods of Producing Active Acquired Immunity

Inoculation with Living Virulent Bacteria.—This form of inducing immunity is impractical and little used. It has been resorted to experimentally with more or less success in animals of diminished susceptibility. Small non-fatal doses are administered and gradually increased. The only instance of the use of this method in man is in Ferran's inoculation against cholera.

Advantage is taken in this method of the relative immunity to infection by other than the usual route of infection. The avenue of infection in this disease is the intestinal tract. By subcutaneous injection of virulent cholera germs a local reaction is produced with slight constitutional disturbances, which, however, is sufficient to produce immunity to the disease.

Inoculation with Living Bacteria of Attenuated Virulence.—In this method of securing immunity the virulence of the causative germ is diminished by various procedures, as by cultivating them in the presence of antiseptics, as in anthrax; by cultivating in high temperature, also used for anthrax vaccines; by drying, as in vaccination for hydrophobia; by passing through an unfavorable host, as in small-pox vaccination. Immunization for anthrax in animals and for small-pox in man are examples of this form of active immunization.

Inoculation with Dead Bacteria (Bacterial Vaccines).—This method of securing immunity is the most practical and of the widest application of perhaps all the methods of securing active immunization. In connection with the use of the opsonic index it is becoming of increasing importance in the prevention of bacterial disease. The most important example of this form of immunization in man is in the vaccination against typhoid fever. It is also used in vaccination against cholera and plague.

Inoculation with Bacterial Toxin.—This method of

producing immunity is little used in man. The most important example of its use is in the immunization of the horse against diphtheria for the production of antitoxin, also in the production of tetanus antitoxin. While the results of this method are usually attributed to the toxin, it is probable that other products of bacterial activity play a part, as the broth upon which the bacteria have been cultivated is separated from the germs by filtration and injected, and in all likelihood contains other substances besides toxin. The employment of tuberculin for the production of immunity is a combination of this method with the use of the dead germs.

CHAPTER XIII

SERUM THERAPY AND VACCINE THERAPY, ANTITOXINS, SERUMS, AND VACCINES

Serum Therapy

Definition.—The treatment of disease by the use of the serum of immunized animals.

Serum therapy may be said to have originated with the discovery of diphtheria and tetanus antitoxin by Behring and Kitasato in 1890, and vaccine therapy by the discovery by Koch, in the same year, of tuberculin. Disastrous results following the use of tuberculin in unselected cases and improper doses led to its abandonment for a time, but antitoxin, being more universally applicable, more specific in its action, and less potent of harm, sprang into immediate and continued use. More careful and painstaking employment of tuberculin with greater knowledge of its action has served to prove its usefulness not alone as a diagnostic measure, but also as a therapeutic agent in the treatment of tuberculosis.

These discoveries, together with the development of vaccine therapy and the opsonic index by Wright, of England, have done more to make medicine an exact science than any other discoveries occurring in a century

past. With the single exception of Ehrlich's "606" in the treatment of syphilis, it may be said that every advance that has been made in the conquest of disease has been along the line of serum therapy, and the hope of the future certainly seems to lie within its magic realm. And who that has watched the dark and gruesome membrane spreading like a pall across the throat of an innocent child, shrivel, and shrink and loose its tenacious hold, that has felt the harried pulse drop into peaceful rhythm, and seen the haunted look leave the eyes of one of these little sufferers, but has felt the magic of its power, has felt that here, among all its vast uncertainties, medicine reigned secure.

ANTITOXIN

The principle upon which the antitoxin treatment of disease depends is the production within the body of an animal affected with disease of certain antibodies which combine chemically with the toxins of the disease, rendering them inert and harmless, hence the term antitoxin. Upon the number and activity of the antibodies present in any particular case depends the outcome of the disease, whether recovery or death, and it is the province of this particular form of serum therapy to assist nature and increase the antibodies by supplying them from an outside source, such outside source being usually the horse, in which they have been cultivated by the systematic injection of increasing doses of the

toxin of the disease, the introduction of the toxins of a disease into a susceptible animal having been found to give rise to an elaboration of antitoxin just as does an attack of the disease.

The **therapeutic action of antitoxin** is essentially a chemical one, depending upon the affinity between the antibodies produced by the cells of the organism and the toxin produced by the germs. The product of such chemical union of toxin and antitoxin is a harmless substance, just as is the product of the chemical action which takes place between the ordinary inorganic poisons and their antidotes, of which we study in toxicology.

It is probable that the toxin also has an affinity for the tissue cells of the body, and combines with them somewhat less readily than with antitoxin. When such union takes place, it becomes necessary for larger quantities of antitoxin to be produced or introduced from without in order to cause the toxin to leave the tissue cells which they tend to destroy, and unite with the antitoxin which renders them inert. We can, therefore, readily understand the necessity for the early administration of antitoxin, and also of the administration of larger doses when not given early.

It is probable that the affinity of toxin for tissue cells is greater in some cases than in others. This is, doubtless, especially true of the toxin of the tetanus germ, for the cells of the central nervous system, and accounts

for the well-established fact that to be of much value tetanus antitoxin must be administered before the advent of convulsions which mark the attack of the poison upon the nervous tissue.

Diphtheria Antitoxin.—*Preparation.*—The method of preparing antitoxin followed by the firm of H. K. Mulford Company may be taken as fairly representative of the process followed by all manufacturers of antitoxin, and is, therefore, described herewith.

Preparation of the Toxin.—A virulent culture of diphtheria germs is grown in pure culture on specially prepared media in incubators and under the most favorable conditions for the production of toxin. After five to seven days' growth trikresol is added to kill the germs, which are then removed by filtration through a Berkefeld filter. The toxin is then tested for strength by determining the minimum fatal dose for a guinea-pig of certain weight in a definite length of time.

Injecting the Horse.—The toxin having been obtained, a small amount is injected into a horse, and the subsequent reaction, temperature, and pulse carefully noted. With the subsidence of the reaction, another and larger dose of the toxin is administered, and this is repeated, gradually increasing the dosage until the horse ceases to react to large doses of toxin or until, in other words, he is immune to the toxin, when his blood will be found to be charged with antitoxin.

It will be noted that the horse is not infected with

diphtheria, the germ having been carefully killed and removed from the toxin before its use. The effect of the injection of the toxin bears out the statement made earlier in this work that the symptoms arising from infection with the various disease germs were due to the toxins produced by the germ, rather than to the presence of the germs themselves in the tissues of the infected animal.

Selection and Care of Horse.—The horse is selected for the production of an antitoxin because he is naturally relatively immune to diphtheria, as well as tuberculosis and other diseases, and furnishes a large quantity of serum. Only healthy animals are selected. They are tested for glanders with mallein, and kept constantly immunized to tetanus by injections of tetanus antitoxin. They are carefully cared for and every precaution exercised to keep them in perfect health.

After the horse has ceased to react to further injections of toxin, he is bled. He is prepared as for a surgical operation. Covered with a sterile sheet, taken into a specially prepared operating-room, where, under the strictest aseptic precautions, the jugular vein is opened and from 3 to 5 quarts of blood removed and received in a covered sterile jar, which is placed in a special room and allowed to clot, when the serum which contains the antibodies can be separated from the clot or fibrin and red corpuscles. After a few days' rest the horse is ready for further toxin administration.

Testing the Serum for Strength.—A standard of strength for antitoxin is established by the government, which provides the manufacturing laboratories with small quantities of test antitoxin for determining the test dose of toxin with which to test the antitoxin manufactured. The amount of test toxin which when mixed with one unit of the test antitoxin furnished by the government will kill a guinea-pig weighing 250 grams in just four days is termed the test dose of toxin. The smallest amount of serum which will save or prolong a 250-gram pig's life just four days when injected with the test dose of toxin will, therefore, be said to contain a unit of antitoxin. If, therefore, it requires $\frac{1}{400}$ c.c. of serum to save the pig's life for four days, the serum will contain 400 units of antitoxin per cubic centimeter. After the strength of the serum has been determined, a small amount of trikresol, a harmless antiseptic, is added to prevent contamination in handling the serum after it leaves the laboratory, and the serum is tested for sterility.

Testing for Bacteria.—A small quantity of the serum is mixed with an equal quantity of sterile bouillon and placed in an incubator, where it is kept for five days, when it is examined microscopically and a portion injected into a guinea-pig, which is watched for several days for symptoms of infection of any kind. Should it not be found sterile, the entire lot is rejected.

Antidiphtheric Globulins or Concentrated Antitoxins.—It has been determined that the real antibodies of the

serum were certain protein-like bodies called globulins, and that by a process of precipitation and filtration these could be separated from the inert elements of the serum, thus reducing the bulk of the dose to be injected and removing some of the objectionable effects which sometimes followed the injection of large doses of the non-concentrated antitoxin, such as urticaria, rashes, etc.

Marketing Antitoxin.—The antitoxin is finally placed in specially devised containers, which are made in the form of a syringe with needle attached, each container holding from 500 to 5000 units of antitoxin. The container is sterilized and packed in an aseptic package which may be opened at the bedside and found ready for instant use.

Dosage and Administration.—As an immunizing dose, that is, such as will prevent one who has been exposed to the disease from becoming infected, 500 to 1000 units may be given, depending upon the age or size of the individual.

A curative dose should never be less than 3000 units, and 5000 had better be given at the beginning of any case if seen early. If the case be not seen until it is well advanced, one should not temporize, but should give 10,000 units at once, and repeat the dose in four to five hours if decided improvement has not occurred.

Large doses can do no harm, and it must be remembered that the longer the disease has been in progress the

more toxin there is in the body that must be neutralized before recovery can occur.

Administration.—The loose skin of the buttocks, between the shoulders, or of the anterior abdominal wall is usually selected as the site of injection. The skin should be thoroughly scrubbed with soap and water, followed by alcohol or, what is more efficient, simply painted at the point of injection with tincture of iodin. The syringe container is removed from its package with sterile hands and its contents injected into the subcutaneous cellular tissue. A drop of collodion may be applied to the needle wound.

Effects.—If the dose has been sufficient within a short time, varying with the severity of the disease and the period of administration, improvement in all the symptoms will be manifest. The temperature will fall, the pulse improve, the membrane cease to advance and begin to loosen up at the borders, being finally coughed up piecemeal or *en masse*. Should such improvement not occur within five or six hours, it is evidence sufficient that the dose has not been large enough, and that another and larger dose should be injected.

Tetanus antitoxin is prepared from the horse in practically the same manner as the diphtheria antitoxin. Tetanus toxin is injected in increasing doses until the horse ceases to react, when he is bled and the serum separated, as in the manufacture of the diphtheria serum.

It is marketed in the syringe containers and also in powder form for use in the treatment of suspected wounds.

Use, Administration, and Dosage.—Wassermann and Takaki found that after mixing tetanus toxin with brain substance it could be injected into animals with impunity. So firmly is the toxin united to the brain cells that it fails to affect the tissues of the animal into which it is injected.

Owing to the peculiar affinity of the tetanus toxin for the cells of the central nervous system, as shown by the above experiment and as borne out by the characteristic symptoms of the disease, the greatest value of the antitoxin lies in its use as a preventive rather than as a curative measure. Therefore, all punctured wounds of a suspicious character, as nail wounds, blank-cartridge wounds, and wounds likely to be contaminated with garden earth or stable manure, should be thoroughly opened to the air, dusted with antitetanic dusting-powder, and a full dose (15,000 units) of the serum injected at the earliest possible moment. This should be repeated in eight or ten days. When the disease is already established, in addition to large and repeated doses subcutaneously, the antitoxin may be introduced into the spinal canal by lumbar puncture, that it may be brought into immediate contact with the toxin in the central nervous system. The wound should be laid open by free incision, and the antitoxin used in and about

the wound in hopes of rendering inert any toxin which has not yet entered the circulatory system.

Antimeningitis Serum.—This serum, like others, is prepared from the horse. In the beginning, alternate injections of dead cultures of diplococcus meningitidis and cultures which have undergone autolysis are injected. Autolysis is a process of self-destruction of the germs which takes place as follows: 10 to 20 c.c. of normal salt solution is poured over a twenty-four-hour culture of the germ. The cultures are separated from the medium by agitation and the flask placed in an incubator for twenty-four hours, when the fluid resulting will be found free from diplococci and to contain only granular débris and solution of diplococci. After several weeks the dead culture, which is alternated with the autolysate, is replaced by living cultures. The injections are continued in increasing doses over a period of four to six months, when the serum of the animal is tested. When it is found active in a dilution of 1: 5000 it is considered fit for use, and the horse is bled and the serum preserved as are other serums.

Action of the Serum.—The mode of action of antimeningitis serum is probably more complicated than that of antidiphtheric serum. It seems to combine the action of a bacterial vaccine with that of an antitoxin. By its opsonic action it increases phagocytosis. The phagocytic destruction of the diplococci sets free their toxin, which the antibodies of the serum are then able

to combine with and render inert. Until the toxins are set free from the germ the antibodies are unable to combine with them, hence the phagocytic destruction of the germs is necessary to the success of the treatment.

Method of Administration, Dosage, etc.—Because the phagocytic action of the serum occurs only in concentrated solutions and because this must precede its antitoxic action, the serum is injected directly into the spinal canal where it can come into direct contact with the germs with a minimum of dilution.

The dose is from 20 to 45 c.c. in adults and 10 to 30 c.c. in children. A similar amount of cerebrospinal fluid is withdrawn by lumbar puncture and the serum introduced in its stead.

The dose should be repeated for three or four consecutive days unless the improvement is so great as to warrant the discontinuance of the treatment. The best guide is the condition of the spinal fluid, which should be examined at frequent intervals. As long as it shows the presence of meningococci the injections should be continued.

Results of Treatment.—When the serum is used early and in sufficient doses the results are extremely gratifying. Coma, headache, delirium, and insomnia disappear at once. The temperature falls perhaps to normal. The paralysis improves or entirely disappears. In fact, the cases which recover are entirely free from the hideous deformities and defects, such as deafness,

blindness, and various paralyses, which attend the cases that recover without the serum. The mortality has been reduced from 65 to 80 per cent. without the use of the serum to 18 to 25 per cent. when the serum has been administered.

Infantile Paralysis.—While the germ of this disease remains unidentified, Flexner has been able to transmit the infection from one monkey to another; has demonstrated that flies may carry the virus from one monkey to another; and, lastly, has perfected a serum with which he is able to render monkeys immune to the virus of the disease which is found to exist in the spinal cord, the nasal secretions, etc., of the animals. This serum is not at this writing perfected for use in the human being, but there seems every reason to believe that it soon will be.

Typhoid Antitoxin.—Chantemesse, of Paris, has succeeded in isolating a typhoid toxin and rendering horses immune by injections of increasing doses of the toxin. He has thus been able to produce an antitoxin with which he claims to have reduced the hospital mortality of typhoid from 18 to 4 per cent.

Owing to the difficulty encountered in the manufacture of this serum and its expense, it is not much used as yet, but there seems no doubt that its use is of considerable value in the treatment of this disease.

Bubonic Plague Antitoxin (Yersin's Serum).—The method of preparation of this serum is very similar to

that used in the manufacture of diphtheria antitoxin. Fresh agar cultures of the Bacillus pestis are sterilized by heat and injected into horses in increasing doses. From six months to a year is required for the production of an active serum. It has been found difficult to standardize, but the endeavor is to produce a serum $\frac{1}{10}$ c.c. of which will protect a mouse from a dose of the germs which kills a control-mouse in three days. The serum is used by injection, the dose being 60 to 150 c.c. Like other antitoxins, it is most efficacious when administered early.

Its use as a prophylactic is attended with most excellent results, but the protection afforded only lasts for fifteen days, so that to be effective over a longer period of time it must be administered at intervals of ten days to two weeks. It has been recommended that it be used in connection with Haffkine's vaccine as a prophylactic measure, a more lasting immunity being thus established.

Vaccine or Opsonic Therapy

Vaccine therapy is based upon the principle of phagocytosis and the opsonic theory of that process. As has been shown in the discussion of immunity, the leukocytes play an important rôle in the protection of the individual against certain diseases. We have also noted that their activity and ability to attack disease germs depends upon the presence in the blood of cer-

tain substances termed opsonins, which prepare the bacteria for destruction by the phagocytes, that is, so act upon the bacteria as to render them susceptible to the action of the phagocytes. Wright discovered that the amount of these opsonins in the blood which, by the way, differ for different bacteria, could be increased for any particular germ by injection into the body of dead cultures of that germ. These dead cultures are called bacterial vaccines. They should not be confused with the vaccines for small-pox and anthrax, which depend upon a different principle, which will be considered later.

The Opsonic Index.—The amount of opsonins for a certain germ present in the blood of an individual may be determined in the following manner:

Equal volumes of blood-serum and of leukocytes from the blood of the individual, which have been washed with normal salt solution, and of emulsion of a culture of the germ in question, are mixed and placed in an incubator for fifteen minutes. We have then phagocytes, germs, and blood-serum containing the opsonins, more or less of which the individual may be possessed. Coverslips of the mixture are then made, stained, and examined under the microscope, when the number of bacteria contained in each leukocyte may be seen and counted. The number of bacteria in 50 or more leukocytes are counted and averaged.

The opsonic index is simply a method of expressing

the relative amount of opsonins in an individual's blood when compared with a normal standard. If the average number of germs contained in a leukocyte in a normal serum were 5, and the average of the individual's blood under examination but 3, his opsonic index would be said to be 3 divided by 5, or $\frac{3}{5}$, or .60.

If under these circumstances a certain number of dead germs be injected into this individual after a certain length of time, an examination of the blood will show an increased number of bacteria in each leukocyte. The opsonic index is said to have been raised.

Like antitoxins, bacterial vaccines are not only of value in the treatment of infections, but they may also be used in the prevention of infection. This is particularly true of typhoid vaccine, which confers a marked degree of immunity to typhoid fever.

Immediately following the administration of a bacteria vaccine there occurs a diminution of the opsonins, which lasts for a variable length of time. This is termed the *negative phase*. This is followed shortly by the increase of opsonins, or the *positive phase*.

It has been contended by some that in protective vaccination this so-called negative phase lays the subject more liable to infection during this time. Experiments, however, have shown that this phase may be practically abolished by using very small initial doses of the vaccine, repeating the vaccinations with larger doses later, that is, in eight to ten days.

BACTERIAL VACCINES

Autogenous Vaccines.—It has been held by some that there are different strains or varieties of the same germ, and that to be of value the vaccine must be made from the identical strain with which the individual is infected by making cultures from the site of infection. Such vaccines are called autogenous vaccines, in contradistinction to stock vaccines which are prepared from other sources.

Stock Vaccines.—These are made from cultures of the germ of other origin than the particular case in which they are intended to be used. They are prepared from pure cultures of different germs of various origin, and are put up in aseptic containers and kept ready for use.

They have the advantage of being ready for immediate use, thus avoiding the loss of time necessary to grow the germ in pure culture from the local infection in the preparation of autogenous vaccines. The question of the superiority of the autogenous vaccines is still unsettled. In the preparation of vaccines the germs are grown in pure culture killed by heat and diluted with normal salt solution until each cubic centimeter contains a definite number of germs which differ for the different bacteria.

Staphylococcus Vaccines.—These have been used with success in treatment of boils, carbuncles, pyorrhea alveolaris, sycosis, etc. Stock vaccines are prepared of Staphylococcus aureus. Staphylococcus albus, and

Staphylococcus citreus, and also of all three combined, for the treatment of infections where all three exist together. Each cubic centimeter contains 400,000,000 bacteria. The dose should be about 100,000,000 to begin with, and increased according to the patient's tolerance. Five to eight days should elapse between doses.

Streptococcus Vaccine.—This has been used with rather meager results. Some benefit is claimed for it in sepsis and in scarlet fever, but the benefit derived from its use is less than from most any of the bacterial vaccines. Doubtless the variety of strains of this germ or its varying behavior under differing conditions may account for the lack of success of vaccine therapy in treating infections with it.

Gonococcus Vaccine.—This has been used with good results in the chronic form and in the complications of this disease, as in arthritis, prostatitis, endocarditis, etc. Its value as an immunizing agent has, fortunately, not been established.

Bubonic Plague Vaccine (Haffkine's Prophylactic).—This vaccine is produced by growing Bacillus pestis upon broth. After the growth has proceeded for a month or six weeks, the culture is sterilized by heating and tested for sterility upon mice, when it is ready for use.

Administration and Dosage.—The dose is from 1 to 3 c.c., administered by injection. The administration

is followed by general and local disturbances similar to those following typhoid vaccination. There is some redness and swelling at the site of injection, fever, nausea, and general malaise, all of which pass off in from twenty-four to thirty-six hours.

Effects.—The immunity conferred is not as great as in typhoid and appears to disappear in about six months. The vaccination should be repeated in ten to fifteen days to make the protection more certain. It is believed that a greater protection is afforded by combining the vaccine with the administration of Yersin's antitoxin.

Typhoid Vaccine.—This is prepared by cultivating a strain of typhoid bacilli of diminished virulence. The culture is killed by heat, a small amount of antiseptic added to prevent contamination in handling, and the culture diluted so that each cubic centimeter represents 1,000,000 dead germs. This is the usual dose, though it may be reduced one-half and repeated in ten or twelve days.

Administration.—The dose is injected subcutaneously in the arm or abdomen, under the usual antiseptic precautions. Following the injection there is some local reaction, accompanied by redness, swelling, and some pain and swelling in the regional lymphatic glands. There are also some constitutional disturbances, varying from a slight indisposition to chills and a temperature of 100° to 100.2° F., with general aching headache, nausea, and diarrhea. They all disappear, however,

in from twelve to twenty-four hours, when the patient feels as well as ever.

The use of the vaccine is becoming a routine measure in the armies of the world, where it is proving most successful, it having been found that less than half as many vaccinated men have the disease as those not vaccinated, while the mortality among those vaccinated who do not contract the disease is less than one-fourth that among the unvaccinated. There is no question but that it will soon become a common procedure among nurses, doctors, travellers, and others whose duties lay them liable to infection.

Tuberculin.—While tuberculin differs in its constituents from the other bacterial vaccines, the principle upon which it acts is practically the same, that is, the increase of the opsonic index and of the resistance of the individual to the tubercle bacillus and its toxins.

The discovery of tuberculin by Koch in 1890 antedates the development of the principle of opsonic therapy by many years. Unguided by subsequent knowledge of this form of treatment, the early advocates of tuberculin in treatment met with disaster in its use, and its employment became restricted to its use as a diagnostic measure. The knowledge gained in the use of bacterial vaccines and opsonic index has enabled us to use tuberculin with advantage in the treatment of tuberculosis.

The method of employing tuberculin as a remedy consists of the administration in the beginning of very

minute doses. These are gradually increased at intervals of three or four days, with the object of increasing the patient's resistance to the tubercle germ and its products until complete immunity is attained.

Various forms of tuberculin are designated, depending upon the method of preparation and the constituents retained.

Old Tuberculin (*Tuberculin O. T.*).—This is the original tuberculin of Koch and contains the toxins and soluble secretions of cultures of tubercle bacilli grown on glycerin bouillon. The cultures are sterilized by heat and the germs removed by filtration.

New Tuberculin (*Tuberculin T. R.*).—This is produced by pulverizing dried tubercle bacilli, dissolving them in salt solution by repeated centrifuging, and decanting the clear liquid. It contains the entire substance of the germ.

Koch's belief is that the use of old tuberculin, consisting as it does of toxin only, produced immunity to the toxin alone, while the proper employment of the new tuberculin produced immunity to both toxin and germ, inasmuch as it represents the entire germ and not the soluble products alone.

The Use of Tuberculin in Treatment.—As will be shown in the study of tuberculin in diagnosis, large doses produce a reaction, with fever, inflammation at the site of injection and the site of the lesion. Such reaction, if profound or if repeated, will do great injury. There-

fore, in the use of this agent, great care must be exercised to avoid producing a reaction. The initial dose is, therefore, placed very low. Thus, of old tuberculin such a dilution is used as will give $\frac{1}{10000}$ mg. in each 2 minims. Two minims of this dilution is mixed with sterile water and injected with a hypodermic syringe under the skin of the forearm or elsewhere, where it may be watched for local reaction. The dose is increased by 2 minims at a dose every four to eight days until 20 minims are injected, when a stronger dilution is used, one containing $\frac{1}{1000}$ mg. to each 2 minims. After the injection the temperature, pulse, and respiration are carefully watched for signs of reaction. Should any occur, the next dose is omitted and the following dose reduced. In this way the patient's tolerance is carefully and gradually increased until no untoward symptoms follow large doses, *i. e.*, as much as 200 mg. It will be seen that the tuberculin treatment, of necessity, must occupy an extended period of time, and, in fact, eight months to a year should be occupied in carrying the patient through the immunizing process.

Small-pox Vaccine.—Vaccine for small-pox was originated by Jenner in 1798. He observed that milkmaids who had pustules upon their hands resembling those upon the cows' udders were immune to small-pox. It is, therefore, perhaps the oldest known application of serum therapy. In principle it differs from all the later biologic remedies.

The principle by which small-pox vaccine protects is doubtless that of a modified attack of the disease through a diminution of the virulence of the causative germ from passage through an unfavorable host, *i. e.*, the cow. In other words, that cow-pox is a modified form of small-pox, its nature and virulence having been changed by the resistance and general character of the tissues of the cow. So that when a human being is inoculated with vaccine or cow-pox, he has a mild local disease in place of the widespread general condition which characterizes small-pox. This mild disturbance is sufficient to establish immunity to the disease for a shorter or longer period of time, varying from three or four to fifteen or twenty years.

The causative germ of small-pox having never been isolated, it is not possible to determine much regarding the mode of action of this product, but years of invariable success and the practical wiping out of small-pox has established its value beyond quibble.

Preparation.—In the preparation of small-pox vaccine young healthy heifers are used. They are carefully examined and tuberculin-tested, and when found healthy are shaved, scrubbed with an antiseptic, and inoculated with cow-pox. The heifers are fed on milk exclusively and kept in separate compartments. When the pustules are fully developed at the end of five to seven days, their contents are collected under strict antiseptic conditions. The contents of the pustules are mixed with

glycerin, macerated, filtered, and preserved in sealed capillary glass tubes, which are broken and their contents ejected by means of a small rubber bulb when used.

Administration.—The skin of the forearm or thigh is thoroughly cleansed with soap and water, followed by alcohol. All traces, however, of alcohol must be removed with sterile water before the vaccine is applied. Having thoroughly cleansed the part, a small abrasion is made either with a small needle or scarifier. This abrasion should be just sufficient to cause an exudation of lymph, care being taken to avoid drawing blood, which would dilute the virus and wash it away, thus preventing a successful vaccination. The virus is then ejected from the tube upon the abrasion, thoroughly rubbed in with the needle or scarifier, and allowed to dry in the air, after which the spot should be protected by a shield or large bunion pad, which protects it from rubbing or injury, but at the same time permits a free circulation of air to the part.

Effects.—In from five to eight days, if the inoculation be successful, the part will become inflamed. There will occur considerable swelling, with pain and more or less swelling and tenderness of the adjacent lymphatic glands. Some fever and general depression are also present. At the site of inoculation there will occur from one to five or six vesicles, which rapidly coalesce and become pustular. These vesicles are umbilicated and resemble small-pox pustules in a minute form. The

vesicle dries in from ten to twelve days and the scab slips off, leaving a typic pitted scar, which is evidence of successful vaccination.

Rabies Vaccine (Pasteur Vaccine).—Pasteur found that the infective agent or its toxin in rabies was located largely in the spinal cord of animals having the disease, and that symptoms of the disease were produced in healthy animals by the introduction of portions of the spinal cord of animals having the disease. He also found that the virulence of the poison was diminished by drying. The longer the infective material was dried, the less its virulence. He then determined that immunity to the disease could be produced by injection of emulsions of the cord containing the infective agent, beginning with a minute dose of the relatively non-virulent material and gradually increasing the dose and virulence of the injected material.

Establishments termed Pasteur institutes are located in all large cities, where the treatment may be carried out. The vaccine is prepared by inoculating rabbits beneath the dura mater with rabic material. The animal develops rabies in six days, when the spinal cord is removed and dried at a temperature of 68° F.

A piece of the cord which has been dried for fourteen days is mixed with sterilized veal broth and injected beneath the skin of the abdomen. On the following day material from a cord thirteen days' old is used, and so on, each day using material a day younger, until fifteen

injections are made. To be of value the immunizing process must be given before the onset of the disease, as soon as possible following the bite of the rabid animal. As the incubation period of hydrophobia is long, extending from three weeks to several years, sufficient time is usually available for treatment.

Recently, enterprising manufacturers have succeeded in perfecting a plan whereby they furnish the vaccine for the entire treatment of a case upon telegraphic notice, shipping the varying strengths in a Caloris bottle, which protects it from changes of temperature. The physician is thus enabled to give the treatment at the patient's home, saving time and the necessity of a long journey to some distant institute.

It should be remembered that this is a purely prophylactic measure, the organism being rendered immune to the disease during the period of incubation, and that after the onset of the symptoms the treatment is useless. No time should, therefore, be lost following a bite by a suspected animal in beginning treatment, either at the nearest Pasteur institute or by means of the vaccine prepared and forwarded to the physician by the dealer in serums and antitoxins.

Mode of Action.—While it is impossible to say with certainty just how immunity is established by this treatment, it is, without doubt, analogous to small-pox vaccination.

A modified form of the disease is produced by injec-

tions of small quantities of virus whose virulence has been attenuated by unfavorable environment, the unfavorable environment in small-pox being the cow; in rabies, the drying under unfavorable atmospheric conditions.

Effects.—It is not possible to obtain an exact estimate of the mortality of hydrophobia before the advent of the vaccination treatment, but it is placed not lower than 10 per cent. Under the vaccine treatment it has been lowered to much less than 1 per cent. Its value is, therefore, unquestioned.

Cholera Vaccine (Haffkine's Cholera Vaccine).—Like small-pox and rabies vaccination, cholera vaccination consists in the inoculation with attenuated cultures of the germ of cholera. Unlike them, however, the germ of the disease has been identified and grown artificially for the production of the vaccine. Two vaccines are used, a weaker and a stronger one. Injections of the virulent germs causes excessive tissue destruction at the site of injection unless the individual has been partially immunized by the injection of the weaker vaccine. The attenuated culture is produced by growing the cholera bacteria upon agar at a temperature of 39° C. in a current of air. The stronger one (and here the method differs radically from all other methods of immunization) is produced by growing the germs on living guinea-pigs. The germs from the peritoneal exudate of the first pig inoculated are incubated for ten

hours at a temperature of 35° C., the temperature most suited to the growth and development of the organism. A second pig is then inoculated and the procedure continued until a culture is obtained which is certainly fatal to a pig in eight hours. A slant of agar is completely inoculated with this virulent culture and grown for twenty-four hours, when it is washed off with broth and diluted up to 8 c.c. One c.c. constitutes a dose. Instead of an attenuated germ we, therefore, have one of increased virulence, which, were it not for the partial immunity already effected in the individual by the weaker vaccine, would most certainly prove fatal. The process is analogous to that used in rendering animals immune to anthrax.

Administration.—The vaccine is injected into the flank. The immunity produced by each injection is attained in five days, so the second injection is given at the end of that time. The results are very good, but not as favorable as in typhoid vaccination.

Recently, Kolle has devised a method of vaccination in which the cultures are killed by heat before injection. The results of this method of vaccination in a recent epidemic of cholera in Japan have been even more favorable than those following the use of Haffkine's method in India.

CHAPTER XIV

SERUM DIAGNOSIS

In addition to their use in the prevention and cure of disease, biologic methods are of great value in diagnosis in certain affections. Among the curative sera which are also of value in diagnosis, tuberculin holds first place.

The Tuberculin Test

As has been noted in the consideration of tuberculin as a remedy when it is injected into an individual free from tuberculosis, there occurs no disturbance of the vital processes, but when administered in any considerable amount to one affected with tuberculosis certain disturbances arise which are referred to as a reaction.

Tuberculin Reaction.—The symptoms characteristic of a tuberculin reaction are rise of temperature to one or two degrees above normal, gastric disturbance, headache, malaise, and what is termed the local reaction, consisting of redness, swelling, and pain at the site of injection and at the site of the disease. One, two, or all of the above symptoms may be present in varying degrees, depending upon the size of the dose, the susceptibility of the individual, and the stage of the disease.

It will be noted that in the use of tuberculin in treat-

ment the dosage is kept low to avoid reaction, gradually increasing as tolerance is established. In its diagnostic use quite large doses are used for the purpose of bringing about the very symptoms it is sought to avoid in its employment as a remedial measure.

Methods of Administering the Tuberculin Test.—*By Injection.*—Old tuberculin is used, and in a weak patient the dose may be about $\frac{1}{10}$ mg., while a robust one should be given as high as 1 mg. The dose is injected under the skin of the back, observing the usual antiseptic precautions. Should no rise of temperature occur, another injection of double the amount of the first dose is given on the third day. In robust patients even larger doses may be given, such as 5 or 10 mg. at the second or third dose, when, if no reaction occurs, the patient may be considered free from active or progressive tuberculosis. A very slight rise of temperature, if accompanied by a local reaction, should be considered positive.

Cutaneous Reaction, Von Pirquet's Test.—This form of the tuberculin test consists of the application of tuberculin to the skin by scarification. The inner side of the forearm is washed with ether. Two drops of old tuberculin are dropped upon the arm about 4 inches apart. The skin is then scarified first between the two drops, then within each of the drops with a special scarifier furnished for the purpose, the amount of abrasion being sufficient to form a scab, but under no circum-

stances great enough to draw blood. A small tuft of cotton is applied to each drop to prevent its flowing away. The center scarification serves the purpose of a control with which to compare the spots to which the tuberculin is applied.

The reaction is considered positive when the tuberculin spots give a hyperemic zone of 4 to 6 mm. with a papule in the center. From such a feeble reaction the reaction may vary in intensity to the production of numerous papules with considerable edema and redness, persisting for several hours.

Ophthalmo-reaction, Wolff-Eisner and Calmette Test.—A drop of dilute tuberculin is instilled in the eye. A positive reaction is characterized by congestion of the palpebral conjunctiva and caruncle, with more or less serofibrinous exudate. The reaction disappears in from twenty-four to forty-eight hours.

The Moro Reaction.—This is a cutaneous reaction produced by applying a tuberculin ointment to the unbroken skin.

A concentrated ointment of tuberculin in anhydrous lanolin is used, and a small amount energetically rubbed into the skin of the abdomen or breast for about a minute.

A positive reaction is characterized by the appearance in from a few to twenty-four or forty-eight hours of a granular or papular eruption of varying intensity, accompanied by more or less itching, and lasting from a few hours to several days. Of these several local tests, the

cutaneous reaction of Von Pirquet and of Moro are the safest and most dependable. They are especially accurate in children. The ophthalmo-reaction is less reliable and is attended with some danger to the eye, especially should there exist some previous inflammatory condition of that organ.

It may be noted in passing that the tuberculin test affords a most efficient means of recognizing tuberculosis in cattle, and is, therefore, of signal importance in efforts to obtain a tuberculosis-free milk-supply for cities and institutions.

The Widal Test for Typhoid Fever

The Widal (or agglutination) test for typhoid fever has been referred to before in this work. It depends upon the presence in the blood of a typhoid patient at a certain stage of the disease of substances termed agglutinins, which when brought in contact with living typhoid bacilli cause them to clump together and cease their ambulatory movements. It is evident, therefore, that the infection must have been present a certain length of time for the Widal test to be positive, that is, until sufficient time has elapsed for the agglutinins of the typhoid germ to have been elaborated in the blood of the patient, or the Widal test will be negative. We find, therefore, that the test is of no practical value until after the first week of the infection. The test is also uncertain because of the fact that the blood of many normal per-

sons possesses the agglutinating property for typhoid germs. It is less marked, however, than in those infected with typhoid, and, therefore, in making the test the blood-serum is diluted to about 1 to 50, when the agglutinating power (of any but the typhoid blood) is too attenuated to manifest itself.

Method of Application.—The lobe of the ear having been cleaned with bichlorid, lysol, or other antiseptic, followed by sterile water, a deep puncture is made with a sterile needle or other pointed instrument. A small amount of blood is collected either in a capillary tube or upon a sterile cover-glass. The blood or, preferably, the serum portion is diluted with normal salt solution or broth to 1 to 25, then a drop of this dilution is mixed with an equal amount of young vigorous typhoid germs from a broth culture, placed in hanging-drop beneath the microscope, and observed.

Should the test be positive, in from one-half to two hours the bacilli will be seen to clump together into masses and lose their motility. The test may be made without the use of the microscope by mixing the culture and serum in a test-tube, when at the end of the usual time a flocculent precipitate will be observed to form in the mixture.

Typhoid Ophthalmo-reaction

This test is similar to the tuberculin ophthalmo-reaction. A solution of $\frac{1}{3}$ to $\frac{1}{2}$ mg. of "typho-protein,"

an extract of typhoid bacilli, is mixed with a drop of water and instilled into the conjunctival sac of a patient suspected of having typhoid fever. If typhoid be present a typic reaction occurs, which is characterized by hyperemia and injection of the palpebral conjunctiva of the lower lid and the caruncle.

In 75 cases of typhoid fever a positive reaction occurred in 71. The reaction takes place within from one to two and a half hours, and persists for from thirty-six to forty-eight hours. The reaction causes no discomfort and appears to be without danger. It is of recent development and has not yet been widely used, but it promises to be one of the most accurate and least complicated of any of the later diagnostic measures.

The Wassermann Test for Syphilis

This test depends upon hemolysis and the so-called deviation and fixation of complement. The process is most too complicated for practical demonstration in a work of this character, but an endeavor will be made to give such an exposition of the subject as will enable one to understand the principle involved in the test.

We have learned that when the blood of an animal of one species is injected into an animal of a different species, the blood of the animal injected acquired power of hemolysis (*i. e.*, ability to destroy the corpuscles) for the blood of the species from whence the injected blood came.

If this hemolytic serum he heated, it loses its hemolytic power, but it may be restored by the addition of a small amount of normal serum from some animal of the same species. Therefore, if red blood-cells be mixed with their inactivated hemolytic serum (*i. e.*, their hemolytic serum which has been heated), and normal serum from some animal of the same species as that from which the hemolytic serum came be added, hemolysis of the red cells will take place. Should there be immune bodies for a certain germ in the added serum, the hemolysis will occur just the same. If, however, there be immune bodies for a certain germ present, and a pure culture of that germ be added to it before it is mixed with the red cells and their inactivated hemolytic serum, the germs become attached to the immune bodies, so fixing the constituents of the serum as to prevent its acting upon the inactivated hemolytic serum to restore its hemolytic power. Hemolysis, therefore, does not occur.

In the Wassermann test for syphilis, red blood-cells of the sheep are mixed with human serum which has been rendered hemolytic for them and inactivated by heat. The addition, now, of human serum from whatever source would, of course, activate the inactivated serum, and hemolysis of the red cells would occur. The serum which is to be tested for syphilis is mixed with an extract of syphilitic fetal liver, pure cultures of the syphilitic germ being unavailable, and then added to the mixture of inactivated hemolytic serum and red cells.

Should there be no syphilis present in the individual and, therefore, no syphilitic antibodies in his blood, the addition of the germs from the syphilitic liver will not affect the serum in the least, and it will proceed to activate the inactivated hemolytic serum, which will then destroy the red cells by hemolysis. The test is then said to be negative.

Should syphilis, however, be present, the syphilitic antibodies will be bound to the syphilitic germs in the fetal liver extract, and the serum thus rendered unable to activate the hemolytic serum in the mixture. Hemolysis would, therefore, not take place, and the test would be positive.

CHAPTER XV

ANAPHYLAXIS

ANY discussion of serum therapy would be incomplete without reference to the phenomenon of anaphylaxis. The name "anaphylaxis" is from the German, and signifies "against protection."

It has been found that the introduction into the blood of an animal of certain protein or albuminous substances, such as blood-serum, bacterial proteins, egg-white, milk, etc., will produce in the animal injected a condition of hypersusceptibility, so that when another injection of the same substance is made after a definite length of time has elapsed for the condition to develop, symptoms of poisoning occur immediately following the injection. The symptoms characterizing this condition are weakness, difficult respiration or asthmatic paroxysms, weakened heart's action, and even death.

The explanation of this condition is that when a foreign protein is introduced into the blood, antibodies for that particular protein, which are either present at the time or are soon formed, begin the destruction of such foreign proteins by decomposition or splitting up into simpler forms of matter.

At a certain stage of decomposition of protein material poisonous products are formed. The process does not stop here, however, but continues, and the poisonous products are further split up into non-poisonous substances. Should a large amount of such poisonous substances be liberated at one time, they might do great damage to the organism before they could be further decomposed and rendered inert. Practically the same process occurs in gastric and intestinal digestion, but the poisonous products are easily further decomposed and rendered inert before they are absorbed into the circulation. Should anything occur to stop digestion at this point the poisons may be absorbed, and cause a condition of auto-intoxication which may be looked upon as analogous to anaphylaxis.

It is probable that upon the introduction of the foreign proteins of horse-serum, in antitoxin, for instance, there are but few antibodies for that particular substance present. Its destruction or breaking up takes place slowly and small amounts of the poisonous products of decomposition are liberated at a time, so that they are soon neutralized without having done any injury. During this process or following the introduction of the foreign protein, large amounts of antibodies for the substance are formed. If now, at the height of the development of these antibodies, usually in about eight to ten days from the first injection, another injection of the same serum be given, it is decomposed so rapidly that a

large amount of the toxic element is produced at once, and the injurious effects of anaphylaxis are manifest.

It is quite likely that many of the symptoms of infection heretofore attributed to toxins are due to anaphylaxis, and the poisons generated in the decomposition of the protoplasm of the germs by antibodies of the infected organism.

The practical lesson of this matter then is that great care should be exercised in the administration of the various antitoxins and serums to avoid the production of anaphylaxis. It would be better, therefore, to administer large initial doses of serum rather than small doses which must needs be repeated. When a second dose of serum becomes necessary, it should follow the first at as short an interval as possible, so that time shall not have elapsed for the development of hypersusceptibility. If it be known that one has had a previous administration of a particular serum at some former illness, another administration of that serum should be undertaken with caution. A very minute dose should be given and the patient closely watched for signs of anaphylaxis. Should these not arise within an hour or so, a full dose may then be given.

PATHOLOGY

PATHOLOGY is the science which treats of disease, its causes, symptoms, and results.

Disease is a condition of a living organism characterized by abnormality in structure, in function, or in both combined.

CHAPTER XVI

ETIOLOGY OF DISEASE

THE causes of disease are numerous. As we have already learned, bacteria and their toxins are the cause of diseases, and in our daily combat with these minute agencies we are prone to lose sight of the other innumerable causes of abnormality of structure and function which exist throughout nature.

Traumatism is the name given to mechanical injury. Besides the ordinary wounds, bruises, contusions of the soft tissues, and fractures of bones, gradual pressure may cause atrophy, and if prolonged or of increased intensity may result in necrosis or gangrene.

Heat.—Local excess of heat produces various lesions, depending upon its intensity and length of application, from simple hyperemia, vesicle formation, to charring

and local necrosis, followed by profound inflammation. Burns involving large surfaces, one-third or more of the body surface, often cause death, doubtless through the production of poisonous products of tissue and blood destruction. General high temperature leads to heat-stroke, sunstroke, insulation, or heat exhaustion. In these conditions there may occur hyperemia and edema or even inflammation of the meninges, which lesions are doubtless due to the production within the body of poisonous substances the result of disturbed metabolic processes.

Cold.—Exposure to extreme degrees of cold gives rise to lesions similar to those produced by heat. Locally, there are produced by excessive low temperature vesiculation and necrosis, similar to burns. In exposure to cold the extremities are first to suffer. The blood being driven inward to maintain the internal bodily heat, local anemia occurs, followed by vascular paralysis, with hyperemia and necrosis. Prolonged exposure to general low temperature leads to gradual obtunding of sensibility and coma.

Cold was formerly believed to be the cause of coryza, pharyngitis, bronchitis, and similar conditions referred to by the term "catching cold." It is now known to be but a predisposing factor, the real cause being infection with certain micro-organisms, the effect of cold doubtless being to lower the resistance and natural protective properties of the body.

Insufficient Air.—A sufficient supply of fresh air is necessary to the proper oxygenation of the blood and the maintenance of health.

Asphyxia.—If the insufficiency be great, asphyxia, a condition of cyanosis, depression, and stupor occur.

Suffocation.—Complete lack of air causes suffocation and death.

Poisons.—*Definition.*—Any substance which introduced into the living organism direct tends to destroy the life or impair the health of that organism.

The effects of poisons depend upon the nature of the poison, the dose, and the nature of the individual. Tolerance or immunity may be produced by repeated ingestion of poisons.

Corrosive Poisons, Escharotics, Caustics.—Such poisons, which are exemplified by various acids, alkalis, mineral poisons, nitrate of silver, etc., cause destruction of the cells with which they come in contact by abstraction of water and coagulation of the albuminous contents of the cell. They cause local lesions similar to burns, with necrosis, sloughing, and surrounding inflammation.

Organic poisons are those which enter the blood and cause extensive lesions to various organs of the body, as the kidneys, liver, gastro-intestinal mucous membrane, heart muscles, blood-vessels, etc. Such poisons are lead, arsenic, phosphorus, and mercury.

Toxins of Bacteria.—As we have seen, the toxins of

bacteria cause various lesions throughout the body. Some act as organic poisons, causing degeneration of heart muscles or kidney structure, as in diphtheria and scarlet fever; while others, as in tetanus, act as nerve poisons.

Venom of Serpents and Insects.—The poisons of snakes and insects produce both local and general lesions. Locally, they give rise to inflammation and necrosis, and, entering the blood, they act as organic poisons, causing extensive destruction of internal organs and the blood itself.

CHAPTER XVII

DISORDERS OF NUTRITION AND METABOLISM

Foods are those substances with which living organisms repair tissues consumed in the wear and tear of life, and furnish the heat and energy for the vital processes.

Inanition and Starvation.—Lack of food causes a diminution of energy and weakness followed by loss of weight, as the various tissues of the body are appropriated to maintain heat and energy. The fat and muscles are consumed first, then the tissues of the liver, bones, and heart. Such a condition may occur either from lack of food or from inability to digest and appropriate food, as in cancer of the stomach or intestines.

Overfeeding.—An increased ingestion of food in persons of great digestive capacity may cause various disorders, first among which may be mentioned obesity or increase of the fatty tissues of the body. Such increase, if deposited about the heart or within the heart muscles, may cause death.

Overfeeding necessarily is a relative matter, as great energy and muscular exertion must call for more food in the same individual than comparative quiet and lack of exercise. Besides fatty deposits in the heart, kidneys, and blood-vessels, overfeeding leads to the condition

termed atheromatous degeneration of the blood-vessels, a condition in which the blood-vessels become hardened and loose their elasticity, thus increasing the blood-pressure. The increased pressure upon the weakened walls of the vessels frequently causes rupture of the walls, especially of the small vessels of the brain, the resulting condition being known as apoplexy. Other results of overfeeding are auto-intoxication from a retention of partially oxidized products of metabolism. Of these, gout is an example. In gout there occur deposits of urates about the joints, with consequent inflammatory reaction.

Glycosuria and Diabetes.—The carbohydrate food-supply is utilized in part by being transformed by the liver into a peculiar form of sugar, called glycogen, which is stored up in the liver cells and muscles of the body and gradually discharged into the blood as needed. Occasionally, when the supply of carbohydrate food is excessive, more glycogen is produced than can be stored up in the muscles and liver, and the excess is discharged through the kidneys. Such a condition is termed glycosuria.

Diabetes.—This is a disease characterized by an increased excretion of urine containing sugar. The cause of this disorder is not known, but it seems to be connected with diseases of the pancreas. Removal of the pancreas in animals causes glycosuria. Just how this is brought about is not clear. The essential facts of the

condition are that the body is not able to appropriate the carbohydrates for the production of energy, and the unused glycogen passes off through the kidneys. The proteins of the tissues are then drawn on for the production of energy, their destruction leading to emaciation, acid intoxication, coma, and death.

Fever.—*Definition.*—Fever is that condition in which the temperature of the body is above 98.6° F. In health there is a constant relation of heat production to heat dissipation, regulated by the nervous system. In sickness the relation is disturbed, due either to increased heat production or to decreased radiation or dissipation, or to greater increase of production than increase in dissipation.

Causes of Fever.—The primary causes of fever may vary greatly, but they probably all depend upon the liberation into the blood of toxic substances. It is the toxins of bacteria that give rise to elevation of temperature in the various infectious diseases, and it is well known that many injuries to the tissues give rise to the production of toxic substances, either as the product of disordered metabolism or of degeneration of tissue cells. These toxic substances may so act upon the nervous system as to cause elevation of temperature. Likewise, toxic substances occur as the result of perverted digestive action and decomposition in the intestinal tract. This is a frequent cause of elevated temperature in infants and children.

It is probable that fever is a conservative process, and that in some way it has to do with the destruction and elimination from the body of the toxic material causing it. That most pathogenic bacteria are unfavorably influenced by high temperature is well known, but whether the temperature of the body in fever is sufficiently high to have any marked influence upon the bacteria themselves is not as yet proved. There is little doubt, however, that such increased temperature has to do with the destruction of the toxic products of bacteria.

CHAPTER XVIII

DISTURBANCES OF CIRCULATION

Hypostatic Congestion.—In extreme weakness of the heart the blood tends to collect in the dependent portions of the body. This condition is known as hypostatic congestion. It occurs in low fevers and frequently results in the formation of ulcerations or bed-sores.

Local Hyperemia.—This is a condition of increased amount of blood in any part of the body. It may be either active or passive. Active hyperemia or arterial hyperemia may be functional, as in the ovaries at the menstrual period, or pathologic, when it is due to dilatation of the arteries from vasomotor activity or from injury and weakening of the walls of the arteries. The hyperemic area is bright red in color, the temperature is elevated, and there is slight swelling.

Passive hyperemia, or venous hyperemia, is due to obstruction of the outflow of the blood from the veins. The obstruction may be due to thickening of the vessel walls, to tumors, or to thrombi within the vessels. Areas the seat of passive hyperemia are dark red in color (cyanotic) and of lowered temperature, followed soon by swelling and edema.

Local anemia, or ischemia, is the condition in which a part of the body contains less than the normal amount of blood. Pressure is the most frequent cause of this condition, though an artery may be obstructed by sclerosis of the vessel walls or by emboli or thrombi. The anemic area is pale, reduced in size and temperature, and functionally less active.

Hemorrhage is the escape of blood from the blood-vessels. It is termed arterial, venous, or capillary, according to the vessel from which the flow of blood occurs. It may occur by diapedesis or extravasation through an intact vessel wall or by rupture of the walls of the vessel.

Diapedesis.—Under certain abnormal conditions red blood-corpuscles may pass through an intact vessel wall and collect in the tissues. This is known as diapedesis. Altered states of the vessel walls and of the blood itself induced by infectious diseases give rise to diapedesis. The small collections of blood in the tissues are called petechiæ. The petechiæ of purpura and the rose spots of typhoid fever are examples of diapedesis.

Emigration.—Under normal conditions a certain number of white blood-corpuscles escape from the capillaries and wander about in the tissues; this is a normal process and is known as emigration.

Hemorrhage from rupture of the vessel walls may occur from—

(1) Traumatism, knife wounds, crushing injuries, etc.

(2) Disease of vessel walls, atheroma, aneurysm, or ulceration, as in phthisis.

(3) Hemophilia, a hereditary tendency to spontaneous hemorrhages.

Classification of Hemorrhages:

Epistaxis, hemorrhage from the nose.

Hemoptysis, hemorrhage from the lungs.

Hematemesis, hemorrhage from the stomach,

Enterorrhagia, hemorrhage from the bowel.

Metrorrhagia, hemorrhage from the uterus between menstrual periods.

Menorrhagia, hemorrhage from the uterus, profuse at menstrual period.

Hematuria, hemorrhage from the urinary organs.

Embolism is the process in which foreign bodies are carried into the blood-stream and become lodged in the smaller capillaries, through which they are not able to pass because of their size. The objects thus deposited are termed emboli.

Kinds of Emboli.—Dust, portions of iron, coal, marble, etc.; portions of blood-clot or thrombi; cells from liver or placenta, tumor-cells or masses; fat-emboli in fracture of bones; air-emboli in wounds of large veins; bacteria and other parasites.

Results of Embolism.—Death may occur from occlusion of the coronary arteries or cerebral vessels. In smaller vessels the results depend upon the nature of the emboli. If bacteria or septic material, a new

septic foci occurs. If aseptic, they may form an infarct.

Infarct.—This term is applied to a wedge-shaped area of tissue which has been deprived of its nutrition by occlusion of an end artery, that is, an artery having little or no arterial anastomosis.

White Infarct.—This form of infarct is due to anemia or to coagulation necrosis.

Hemorrhagic Infarct.—In some cases the anemic area becomes filled with blood from back flow from the veins or from capillary anastomosis; the condition is then known as hemorrhagic or red infarct.

Thrombosis is the process of coagulation of blood within the heart or vessels. The clot thus formed is called a thrombus. Blood will not clot within the vessels unless one or more of the following causes be present: First, slowing of the blood-current, as in exhaustive illnesses and fevers, or from pressure upon the vessel walls from tumors or growths; second, changes in the vessel walls, as from injuries, atheroma, or inflammation; third, alteration in the blood, which increases the tendency toward coagulation.

Results of Thrombosis.—Collateral circulation may be established, when no results will follow, or, no collateral circulation being established, degeneration and necrosis may occur. Organization may occur and the thrombus be converted into connective tissue. Simple softening may occur and portions of the thrombus, becoming

detached, form emboli. Purulent softening may occur, followed by infectious emboli and pyemia.

Edema or **dropsy** is that condition in which there is an excessive amount of fluid in the tissues. The most important causes of edema are: Increased blood-pressure, the result usually of heart disease or the pressure of tumors upon the veins, etc. The fluid constituents of the blood are thus forced through the vessel walls into the tissues. Another cause is found in increased permeability of the vessel walls in Bright's disease, which causes extensive changes in the vessel walls. The tissues the seat of edema present a pale, swollen appearance, of doughy feeling, and upon pressure an indentation remains behind.

Ascites.—Edema of the abdominal cavity is known as ascites.

Hydrothorax is the term applied to edema of the thoracic cavity.

Inflammatory edema refers to edema around an inflamed area.

CHAPTER XIX

RETROGRADE PROCESSES

Atrophy.—This is a condition in which a fully developed organ or part undergoes a uniform diminution in size, due to a disappearance of the elemental cells of the organ or part.

Hypoplasia is a condition in which from lack of development an organ remains undersized or rudimentary.

The causes of atrophy may be pathologic, from disease or other injurious agency, as in atrophy of the testicle after orchitis; or it may be physiologic, as the atrophy of organs after their period of functional activity is passed, as the atrophy of the thymus at puberty, the ovaries and mammæ at the menopause.

Degeneration.—The term "degeneration" is applied to a condition in which a tissue is converted into tissue of a different character and lower vitality.

Cloudy Swelling.—This form of degeneration occurs most frequently in the kidney and liver. The normal cells become swollen, cloudy, and vacuolated. It is caused by fever, poisons, bacterial toxins, etc.

Fatty Degeneration.—Under the influence of various toxic substances, as lead, mercury, arsenic, bacterial poi-

sons, anemia, cachexia, etc., normal tissue cells are converted into fatty tissue. This occurs most frequently in the heart muscle, the tissues of the kidney, liver, blood-vessels, and nervous system. Other degenerations are amyloid, mucoid, hyaline.

Necrosis is the term used to define the condition of local tissue death.

The causes of necrosis are trauma or chemical injury, as in crushing injuries and acid burns; thermal injuries, as in freezing or burning; nutritional or circulatory disturbances, as thrombosis, embolism, atheroma, cachexia, senility, and diabetes.

Coagulation Necrosis.—This is a form of tissue death in which there occurs a coagulation of the dead tissue similar to the coagulation of blood. It is more often the result of bacterial poisons, though it occurs as a result of chemical irritants and thermal injuries.

Liquefaction Necrosis.—In this form of tissue death the dead tissues become liquefied. In coagulation necrosis the dead tissues become firmer and stiffer, while in liquefaction necrosis they become fluid or semifluid. It occurs most frequently in the brain, less often in the skin and heart muscle.

Caseation.—This is the term applied to the form of necrosis in which the dead tissue is transformed into a cheese-like substance. It is exemplified in the cheese-like degeneration which takes place in the tubercle of tuberculosis.

PLATE III

Senile dry gangrene of the lower extremity (Hektoen in "American Text-book of Pathology").

Gangrene may be defined as necrosis with putrefaction of the necrotic tissue.

Dry gangrene is the form in which the tissues become mummified. It occurs chiefly in parts of the body exposed to the air, and is exemplified in senile gangrene of the extremities, which is caused by failure of the blood-supply to the extremities, and also in gangrene which follows freezing of the extremities.

Black Gangrene.—When the gangrene has been preceded by congestion, the dead blood colors the necrotic tissue black, giving rise to the term black gangrene.

White Gangrene.—When the part is anemic at the time of death and is not afterward permeated with blood, it remains pale, and the condition is called white gangrene.

Moist Gangrene.—This form of gangrene occurs in the presence of liquids, and, therefore, is found chiefly in deep-seated tissues, as the lungs, bowels, appendix, kidneys, etc. The necrosed tissue remains soft in these localities and often liquefies.

CHAPTER XX

INFLAMMATION AND PROCESSES OF REPAIR

INFLAMMATION

INFLAMMATION is essentially a local tissue degeneration combined with exudation from the blood-vessels, caused by some injurious agency, with which is associated, earlier or later, tissue proliferation, leading to regeneration or hypertrophy (Ziegler).

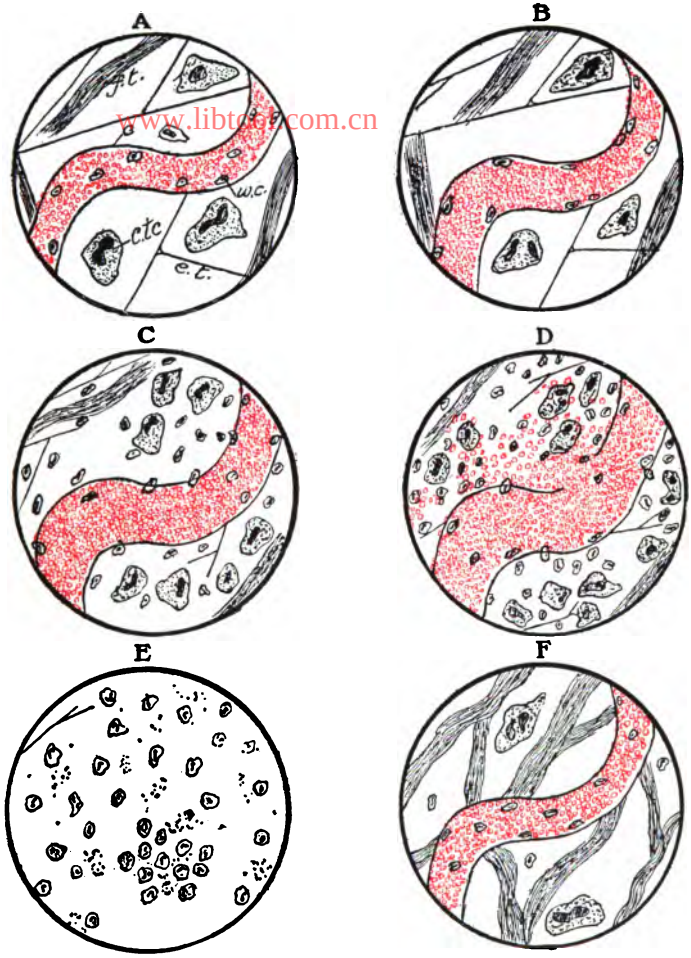
The four cardinal symptoms of inflammation, as designated by Celsus, are: *Calor* (heat), *rubor* (redness), *tumor* (swelling), *dolor* (pain), to which was added later *functio læsa* (altered function).

Causes of Inflammation.—*Traumatic*, as blows and mechanical injuries. *Chemical*, as stings of insects, ivy-poisoning, acid injuries, etc. *Thermal*, as heat and cold. *Specific*, as bacteria erysipelas, peritonitis, etc.

CONSIDERATION OF THE PROCESSES OF INFLAMMATION

Hyperemia.—The onset of inflammation is marked by dilation of the blood-vessels and a quickening of the blood-current, which accounts for the heat and redness. This is quickly followed by slowing of the current and exudation.

PLATE IV



Changes in the blood-vessels and tissues due to inflammation. (From Russell Howard's "Surgical Nursing," by permission of the author.)

A. Normal capillary blood-vessel and connective tissue: *f.t.*, Fibrous tissue; *c.tc*, connective-tissue cell; *w.c.*, white blood corpuscle; *c.*, capillary; *e.t.*, elastic tissue.

B. First change. Dilatation and congestion of blood-vessel; the white cells arranged along the sides of the vessel wall; exudation of serum.

C. Second change. Blood-vessel dilated and congested; exudation of white cells (phagocytes); multiplication of fixed connective-tissue cells; fibrous and elastic tissue indistinct.

D. Third change. Rupture of the congested vessel and escape of red corpuscles; multiplication of connective-tissue cells; normal tissue very indistinct.

E. Pus. Breaking down of the whole tissue, due to the presence of micro-organisms; suppuration.

F. Chronic inflammation. Blood-vessel small; great increase of fibrous tissue.

Exudation.—As the blood-current slows down the white blood-corpuscles gather along the vessel walls, through which they presently begin to pass, prompted, no doubt, by a change in the walls of the vessels and an attraction for the irritant that is causing the inflammatory reaction. Along with this migration of the leukocytes there occurs an exudation of inflammatory lymph which is modified blood-serum. This infiltration of the tissues with leukocytes and lymph is the origin of the "tumor" or swelling.

Degenerative Changes

Any irritant sufficient to cause inflammation causes more or less tissue degeneration or necrosis, so we have as a part of inflammation more or less necrosis.

Proliferation.—In all inflammation of any extent there occurs a certain amount of connective-tissue cell proliferation. It is probable that this is an attempt on the part of nature to supply new tissue to take the place of that injured or destroyed by the inflammatory process.

Resolution.—The recovery from an inflammatory process occurs more or less as follows: The leukocytes re-enter the blood-vessels or pass into the lymph-vessels. The liquid exudate is absorbed by the blood-vessels or lymphatics; the necrotic tissue is either removed by the phagocytes or becomes liquefied and is absorbed. The regenerated tissue remains and takes the place of the destroyed tissue, forming what is termed a scar.

Cicatrix or Scar.—The replacement of tissue destroyed by inflammation or otherwise by a peculiar form of connective tissue, called scar tissue, is called cicatrization, and the result is called a scar or cicatrix.

Suppuration.—This is an inflammatory condition in which necrotic tissue and inflammatory exudate are liquefied by the action of pyogenic micro-organisms.

Pus.—The liquid resulting from the process of suppuration is called pus. It is composed of white blood-corpuscles, broken-down tissue cells, serum, bacteria, etc.

Abscess.—When a circumscribed area of suppuration occurs within the substance of a tissue or an organ, the lesion is termed an abscess. An abscess may, therefore, be defined as a circumscribed collection of pus surrounded by a restraining wall of proliferative tissue, which has been referred to as "the pyogenic membrane," from the mistaken idea that it was concerned in the production of the contents of the abscess.

Diffuse Cellulitis or Purulent Infiltration.—When suppuration within a tissue or organ does not become circumscribed, but spreads through the substance of the tissue or organ, the condition is known as diffuse cellulitis or purulent infiltration. This condition is usually due to streptococcus infection.

Ulcer.—Suppurative conditions upon the surface of an organ or tissue (*i. e.*, upon the skin or mucous membranes) give rise to erosions termed ulcers. An ulcer

corresponds histologically to an abscess, the outer wall of which is missing. The base of the ulcer, being composed of granulation tissue, corresponds to the pyogenic membrane of an abscess.

Sinus.—A sinus is the tortuous track by which a deep-seated abscess opens upon the surface. A sinus cannot heal until the suppurating surface or cavity which it drains ceases to suppurate.

Wound Repair: Regeneration

Healing by First Intention.—When the lips of a clean aseptic wound are brought in apposition, proliferative connective-tissue cells join the apposing walls, proliferative epithelial cells close over the surface, and the wound is said to have healed by first intention.

Healing by Second Intention.—Should the walls of the wound not be brought into apposition, or be exposed to irritants, or become infected, granulations spring up on the apposing surfaces, filling up the intervening space. This granulation tissue is gradually converted into fibrous tissue, the old epithelial cells at the edges of the wound proliferate and cover over the surface of the new-formed fibrous tissue, and the wound is said to have healed by granulation or second intention.

Progressive Processes

Hypertrophy.—The term "hypertrophy" is used to designate that pathologic condition in which a tissue or

organ increases in size through the increase in size or multiplication of its elemental cells. Thus the structure of the hypertrophied tissue does not differ materially from normal tissue.

Simple hypertrophy is due to an increase in size of the individual cells of the organ, and is exemplified in the hypertrophy of the pregnant uterus and in compensatory hypertrophy of the heart.

Hyperplasia or **numeric hypertrophy** consists of an increase in the number, but not in the size, of the individual cells composing an organ or tissue.

CHAPTER XXI

TUMORS

A TUMOR may be described as an atypic non-inflammatory proliferation of a tissue of embryonal or postnatal origin (Hektoen).

Causes of Tumor Formation.—Though many theories have been advanced in explanation of the phenomena of tumor growth, a definite etiology is as yet unknown. Virchow held that tumors were due to external irritation, but while there occur frequent instances of tumors following irritation, such as smokers' cancer of the lip and carcinoma of the breast following irritation and inflammation of the nipple, there are too many instances of tumors occurring without previous irritation for the acceptance of this theory. Cohnheim held that all tumors were due to misplaced islands of embryonic tissue (embryonic rests), which under favorable conditions set up growth and development independent of the tissues in which they were planted. It is true that certain tumors most certainly do originate in this way, but, like the irritation theory, it cannot be held applicable to all tumor growths.

The infectious theory of the origin of tumors is also advocated, but the fact remains that the absolute cause of tumors is as yet unknown.

Structure.—The elemental cells of tumors do not differ greatly from normal cells of a like kind, but the relations of the cells to each other and of the tissues composing the tumor are invariably atypic.

Classification of Tumors.—Tumors are sometimes classified according to their embryonic origin, those developing from the middle embryonic layer or mesoblast being termed connective-tissue tumors, while those developing from the hypoblastic or epiblastic layers, being composed of epithelium as well as connective tissue, are called epithelial tumors.

Tumors are also classified, according to their danger to life, as benign and malignant tumors.

Benign tumors are those which do not spread or recur after removal, do not affect the general health, and are only dangerous secondarily through pressure on vital organs or hemorrhage.

Malignant tumors affect the general health, usually causing death eventually. They tend to recur after removal and spread to other parts by metastasis.

CONNECTIVE-TISSUE TUMORS

Fibroma.—A fibroma is a benign tumor composed of fibrous tissue. Springing from pre-existing connective tissue, fibromata are found in numerous localities, the

more important examples being fibromata of the uterus, ovaries, and mammary gland. Less frequently they spring from the submucous connective tissue of the nose and the subcutaneous connective tissue of the skin.

Myxoma.—Myxomata are benign tumors composed largely of a form of mucous tissue having a connective-tissue framework and an intercellular substance of a gelatinous nature. Myxomata occur in submucous and subcutaneous connective tissue and in the mammary gland, brain, spinal cord, and nerves.

Lipoma.—Lipomata are benign tumors composed of adipose tissue. The growths occur in the subcutaneous tissue of the back, buttocks, thighs, and abdomen, less frequently in the kidneys, mammary gland, and brain.

Chondroma.—Chondromata are benign tumors composed almost exclusively of cartilage. A small amount of connective tissue acts as a framework for the blood-vessels of the growth. Chondromata usually occur in bone periosteum or cartilage, but are occasionally found in the testicle, ovary, and parotid gland, where their presence must be accounted for on the theory of a misplaced matrix of cartilaginous tissue.

Osteoma.—Osteomata are benign tumors composed of bone. They are found usually in connection with bony or cartilaginous tissue, though, like chondromata, they also occur in the testicle, ovary, and parotid gland. The most common example of osteoma is the exostosis

occurring at the metatarsophalangeal joint in connection with the affection termed *bunion*.

Angioma.—Angiomata are benign tumors composed of blood- or lymph-vessels. Those composed of blood-vessels are called hemangiomata, while those composed of lymph-vessels are termed lymphangiomata. Strictly speaking, these are usually but enlargements and dilations of existing vessels. In some instances, however, actual proliferation of vessels occurs, especially in hemangiomata.

Vascular nevi, or Port wine birth-marks, are angiomata of congenital origin.

Myoma.—Myomata are benign tumors composed almost exclusively of muscular fibers.

Leiomyomata are composed of smooth muscular fibers, and occur most frequently in the uterus.

Rhabdomyomata are composed of striated muscular fibers, and occur in the kidney, uterus, vagina, muscles, etc.

Glioma.—Gliomata are benign tumors composed of neuroglia or the cells of the stroma of the central nervous system. These growths occur in the brain and spinal cord. While they are benign tumors, they are often dangerous to life because of their location.

Neuroma.—Neuromata are benign tumors composed of nerve-fibers. True neuromata are rare. False neuromata (fibrous growths springing from the endoneurium or perineurium of nerves) are, in reality, a form of

fibroma. The most important of these forms of growth are the amputation neuromata, occurring at the site of amputations. They also occur along the course of nerves, independent of amputation or injury.

Lymphadenoma.—This is a malignant form of growth composed of lymphadenoid tissue. It occurs in the lymphatic glands and other adenoid tissues. The exact relation of this form of tumor growth to Hodgkin's disease is not well understood. It is probably one manifestation of this disease.

Lymphosarcoma.—Lymphosarcomata are simply the forms of lymphadenomata which partake of the character of sarcoma. It is doubtful if there exists any material distinction between lymphadenoma and lymphosarcoma. They are both probably forms of sarcoma.

Sarcoma.—Sarcomata are malignant growths composed of connective tissue closely resembling the embryonal type, having an abundance of cells and little intercellular substance. Sarcomata always arise from mesoblastic tissue, as bone, cartilage, or connective tissue. They occur in the bones, periosteum, brain, liver, lungs, and intestines. They most frequently affect children or young adults. They form metastases through the circulation, recur after operation, and are always fatal.

Various forms are designated according to their histologic structure, such as spindle-celled sarcoma,

giant-celled sarcoma, small and large round-celled sarcoma.

Lymphosarcoma.	Melanosarcoma.
Alveolar sarcoma.	Chloroma.
Tubular sarcoma.	Myxosarcoma.
Angiosarcoma.	Psammoma.
Sarcomatous cylindroma.	Osteosarcoma.

Adenoma.—Adenomata are benign tumors which spring from glands and present a more or less typic glandular structure. Adenomata occur in the skin, mucous membranes, mammary glands, liver, kidneys, and ovaries, wherever glandular tissue exists. While they are essentially benign in their nature, those of certain localities, particularly of the uterus and stomach, are prone to carcinomatous degeneration.

Carcinoma (Cancer).—Carcinomata are malignant epithelial tumors. They always arise from epithelial structures, as the skin, mucous membrane, glands, etc., and, spreading rapidly by infiltration and metastasis, are usually rapidly fatal. They occur most frequently in those past middle age, though no age is exempt from their devastation. Many of the lower animals are susceptible, including rats and mice, and most of the experimental work on cancer has been done on rats and mice. It has been determined that in rare instances carcinomata spontaneously disappear, after which the organism

is immune to this growth. This occurs in mice, where tumors are transferred from one mouse to another, and it has been established that recovery also occurs, though rarely, in human beings.

Ascitic fluid from an individual who had recovered from cancer has been found to retard the growth and cause the disappearance of cancer in another individual into whom it was injected. Thus, while the cause of cancer remains a mystery, the conquest of the age-old scourge seems about to be realized.

Cancer occurs in all parts of the body where epithelial tissue exists. Among the more frequent seats of the growth may be named the skin, stomach, intestines, esophagus, tongue, rectum, mammary gland, ovaries, liver, kidney, prostate, and testicle.

Histologic Characteristics of Cancer.—In sarcoma the epithelial cells are distributed fairly uniformly through the stroma, each cell being surrounded by connective-tissue fibrillæ, the connective tissue preponderating. In carcinomata the epithelial cells preponderate and are gathered in groups or cell-nests, which are surrounded by a stroma of connective tissue. This alveolar structure is always characteristic of carcinoma, no stroma penetrating between the individual cells, as in sarcoma. These epithelial plugs infiltrate the surrounding tissue, invade the lymph-channels, and are soon found in the regional lymph-glands. From the glands the general circulation is invaded and metastatic tumors occur in distant

organs or tissues. Rarely the tumor cells pass directly into the circulation. This is more characteristic, however, of sarcoma. After attaining a certain size or stage of development, degeneration of cancer occurs. This may take the form of mucoid, colloid, hyalin, or amyloid degeneration or necrosis, which is probably hastened by infection. The degenerative changes, however, never equal the growth of the tumor.

Varieties of Cancer.—*Flat-celled Carcinoma.*—This develops from all squamous or stratified epithelium.

Melanocarcinoma.—This is a flat-celled carcinoma containing pigment. It develops from squamous or stratified epithelium.

Columnar-celled Carcinoma.—This arises from tissue containing cylindric epithelium.

Colloid Carcinoma.—This is a columnar-celled carcinoma in which the cancer cells have undergone colloid degeneration, usually occurring in the digestive tract.

Adenocarcinoma.—This tumor develops from glandular tissue and simulates glandular tissue in its structure.

This is divided into *simple*, in which the cells and stroma are about equal; *medullary*, in which the cells predominate; *scirrhus*, in which the stroma is in excess. The scirrhous variety is found in the breast, stomach, ovaries, and testicle.

Giant-celled Carcinoma.—A rare form in which the cells attain a large size from various causes.

Teratoma and Teratoid Tumors

These are tumors composed of all three layers of the embryo—hypoblast, mesoblast, and epiblast.

These tumors, may, in general, be looked upon as arising from misplaced fetal remnants.

Dermoid Cyst.—This is a benign tumor, though sometimes prone to carcinomatous degeneration. It is composed of a connective-tissue membrane lined with skin. Its contents are the various appendages of the skin, such as hairs, sebaceous glands, and occasionally teeth. They grow very slowly and may remain latent, varying in size from that of a pea to enormous masses. They are found most frequently in the ovaries, less frequently in the testicles, peritoneum, membranes of the brain, in the neck, floor of the mouth, and about the eye.

Bigeminal Teratoma.—In this form of tumor we have the implantation of an ovum or fetus upon or within the tissues of another fetus. The misplaced organism may remain dormant, while the one upon which it is implanted develops slightly or to considerable extent, giving rise to various monsters. Where the extra fetus is enclosed within another, it is termed *endogenous* teratoma; where two are fused, one developing only in part, it is called *ectogenous* teratoma.

CHAPTER XXII

PARASITES AND DISEASE (VEGETABLE PARASITES)

Bacteria.—We have learned in our study of bacteriology that bacteria are an important cause of disease processes. We will now, in pathology, consider the diseases of which they are the cause, and the alterations in structure and function of the organs and tissues affected by their growth and multiplication within the body.

Local Effects Upon the Tissues of Bacterial Growth.—The local effects of bacterial activity may be either mechanical or histologic.

Mechanically, the clumps of bacteria may obliterate small vessels, leading to thrombosis, necrosis, or infarct. By the production of membranes, as in diphtheria, they may occlude the air-passages, causing suffocation.

The histologic effects of bacterial growth are both proliferative and degenerative. Among the proliferative processes may be mentioned the formation of tumor-like growths, as gumma in syphilis, tubercle in tuberculosis, the nodular formation in leprosy, and the proliferative changes in the vessel walls occurring in late syphilis. Of the degenerative changes, necrosis is the most important, as exemplified in the various ul-

cerations, in phagedenic ulcer, and the local tissue death of dental caries. Degenerative changes also occur secondary to many of the proliferative processes, as in the necrosis of tubercles.

The effects of the products of bacteria are sometimes local, but they are more often of a general nature. The toxins may cause local suppuration or they may enter the circulation and become localized in some special tissue, as the localization of tetanus toxin in the cells of the central nervous system, to which it is highly destructive, though harmless to other tissues of the body. Other toxins have a selective action also, as the preference of the diphtheria toxin for involuntary muscle cells.

Diseases Due to Bacteria

Suppurative Diseases (Furunculosis, Abscess, Osteomyelitis, Otitis Media, Mastoiditis, etc.)

Definition.—Diseases characterized by the formation of pus.

Etiology.—The usual cause of these disorders is the introduction into the tissues of the Staphylococcus albus, aureus, and citreus, streptococcus, under certain conditions the pneumococcus, and the gonococcus. The typhoid bacillus and the colon bacillus give rise to suppurative diseases, and they are sometimes present as mixed infections, with the ordinary pus microbes.

A lowered resistance, debility, anemia, and lowered opsonic index are contributory causes. That these

germs may cause such diseases has been abundantly proved by injections of cultures of the causative germ in both human beings and animals.

GONORRHEA

Definition.—A contagious catarrhal inflammation of the genital mucous membrane due to the gonococcus.

Etiology.—The specific cause of this disease is infection with the gonococcus. This has been proved by direct inoculation with the germ. Infection practically always occurs through sexual intercourse, although instances of innocent infection do occur from use of towels, clothing, chambers, etc.

Morbid Anatomy.—The organism causes a suppurative inflammation of the mucous surfaces with which it comes in contact. The germs tend to penetrate deeply into the surrounding tissue, sometimes giving rise to peri-urethral abscess. It sometimes enters the blood and, locating in the heart, induces endocarditis in the joints, causing arthritis, etc.

Morbid Physiology.—The disturbances of function occurring in this disease are due largely to the germs themselves rather than to their toxins, which are not capable of producing the characteristic symptoms of the disease.

LOBAR PNEUMONIA

Definition.—An acute infectious disease characterized by inflammation of the lungs, toxemia, and fever.

Etiology.—The exciting cause of this disease is the Diplococcus pneumoniæ, its presence having been demonstrated in a large proportion of the cases investigated. That predisposing causes and the virulence of the germ are factors in the causation of the disease is shown by the fact that the germ is found in the air-passages of healthy individuals. Of predisposing causes, age plays an important part, the majority of cases occurring in infancy and old age. Lowered vitality from exposure, overwork, poor food, alcoholism, previous debilitating diseases, as influenza, typhoid, etc., injuries to chest, and ether-anesthesia are also predisposing factors.

Morbid Anatomy.—In this disease, instead of isolated areas, the entire lobe of the lung is affected. The inflammatory process is divided into four stages, which are designated as engorgement, red hepatization, gray hepatization, and resolution.

Engorgement.—In this stage of the disease the lung tissue is deep red in color, the capillaries are dilated and tortuous. The alveoli contain red blood-corpuscles, round cells, and detached epithelial cells, but are not as yet completely occluded.

Red Hepatization.—In this stage the surface shows the indentation of the ribs. Its consistency is firm and friable. The alveoli are completely filled with fibrin, red and white blood-cells, epithelium, bacteria, and granular débris. The bronchial mucous membrane is reddened and engorged, the smaller bronchi often con-

tain fibrous plugs. The cut surface of the lung presents a granular, reddish-brown appearance resembling liver tissue, hence the name hepatization.

Gray Hepatization.—In this stage the tissue has changed from reddish-brown to grayish-white in color. The air-cells are filled with leukocytes, the fibrin and red blood-cells having largely disappeared.

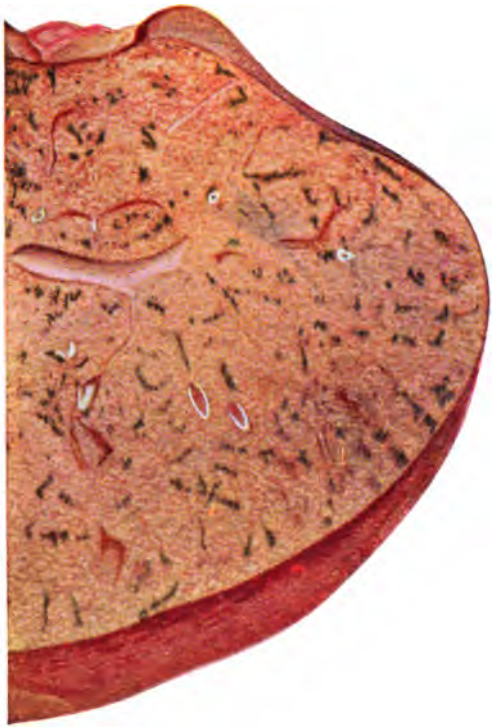
Resolution.—In this stage liquefaction of the alveolar contents takes place partially through autolytic digestion and partially by mucoid and fatty degeneration. The liquefied mass is expectorated, absorbed, and excreted by the kidneys, air again enters the alveoli, and the parts gradually approach the normal.

Morbid Physiology.—Interference with respiratory function is proportionate to the amount of the lung involved and the pain and fever present. The absorption of toxins causes profound systemic disturbances, evidenced by prostration, high temperature, weak heart action and low blood-pressure, and leukocytosis. The diplococcus may enter the blood and give rise to complications in distant organs, as endocarditis, pericarditis, and meningitis.

DIPHTHERIA

Definition.—An acute infectious and contagious disease due to the Klebs-Löffler bacillus, characterized by a fibrous exudate at the site of infection and constitutional symptoms due to toxins produced at the site of the lesion.

PLATE V.



Croupous pneumonia, stage of gray hepatization (Bollinger).

Etiology.—The exciting cause is the diphtheria bacillus. The frequent presence of the germ in healthy throats indicates the necessity of predisposing causes, among which are lowered resistance and personal susceptibility, enlarged tonsils, pharyngitis, laryngitis, etc. Infection may occur from food, especially milk, from books, toys, from persons in contact with the disease, and from healthy carriers of the bacillus. Age is important. Sucklings are very slightly susceptible. From the second to the fifth year the susceptibility increases, then gradually decreases.

Morbid Anatomy.—This is essentially a local disease of the larynx, pharynx, or nose, with systemic and visceral lesions due to the absorption of the toxins. Locally there is produced upon the mucous membrane at the site of infection a false membrane. There is necrosis of the epithelium, followed by an inflammatory exudate rich in fibrin, which, in conjunction with the dead epithelial cells, form the false membrane. The germs grow and develop upon the necrotic tissue and not upon the living tissue. Removal of the false membrane leaves a raw and bleeding surface beneath, the depth to which the tissues are affected depending upon the amount of necrosis. This membrane may block the nasal passages, extend to the conjunctiva, and through the Eustachian tubes to the middle ear.

It may block the larynx or extend into the trachea or bronchi. The internal lesions are due to the toxin, as

the germs are not usually found in the circulation. They consist of fatty degeneration of the heart muscle and acute interstitial myositis. The kidneys are also affected, the lesions varying from simple degeneration to intense nephritis. The liver and spleen show degenerative changes, with foci of necrosis. Degeneration of the peripheral nerves and neuritis also occurs.

Morbid Physiology.—While deglutition and interference with respiration may occur from the presence of the membrane and inflammatory reaction, the lesion is purely a local one, and the systemic disturbances (chill, fever, prostration, and visceral lesions) are caused by the toxin, which is very soluble and highly toxic. Introduction of the toxin into animals reproduces practically all the general manifestations of the disease. Various degrees of susceptibility to the toxin and also to the growth of the germ exist, so that frequently an exaggerated local lesion is accompanied by slight constitutional disturbances and vice versâ. An attack confers temporary immunity.

CEREBROSPINAL FEVER

Definition.—An acute infectious disease caused by the meningococcus and characterized by inflammation of the cerebrospinal meninges and a clinical course of great irregularity.

Etiology.—Epidemics of this disease are localized, and occur with greater frequency in the country than

in cities. Infection must depend upon a particular susceptibility, as it is rare to have more than one case in a home, and carriers are frequently found who, though perfectly healthy themselves, carry the germs in their throats or noses. It seems not to be contagious. Heat, overexertion, squalor, and want appear to be predisposing causes. Sporadic cases occur at all times. Flexner has demonstrated by animal inoculations that the meningococcus is the cause of the disease, and has perfected a curative serum.

Morbid Anatomy.—The brain and cord show intense congestion, accompanied in cases that have lasted a week by a fibropurulent exudate most marked at the base of the brain. Sometimes the entire cortex may be covered with exudate. The cerebrospinal fluid is turbid and contains the meningococcus. In chronic cases there may be general thickening of the meninges. Petechia of the skin may occur, giving to the disease the name spotted fever. Other organs of the body are but slightly affected, though pericarditis, pleurisy, and parotitis may occur.

Morbid Physiology.—Because of the location of the infectious process in the brain and spinal cord the perversion of function is widespread. There are chills, fever, vomiting, headache, convulsions, and paralysis. Mental disturbances, delirium, mania, stupor, or coma may be present. Increased leukocytosis is a constant and persistent condition. Cases which recover are usually mentally defective or suffer from various paralyses,

blindness, deafness, etc. Recovery after the use of Flexner's serum is not accompanied by these defects.

TYPHOID FEVER

Definition.—An infectious disease caused by the Bacillus typhosus and characterized by hyperplasia and ulceration of the intestinal lymph-follicles, and swelling of the mesenteric glands and spleen.

Etiology.—The specific cause is the typhoid germ, which gains entrance to the body through the alimentary canal, locating in the intestinal glands. Predisposing causes are lowered vitality from any cause. The greatest susceptibility exists between the ages of fifteen and twenty-five. Infants are rarely attacked. The most frequent sources of infection are milk and water, though any food-product which is eaten raw may convey the infection.

Flies are probably the greatest disseminators of infection. One attack usually confers immunity for life, but a second and even a third attack may occur. The germs may persist in the bile-passages and intestines of persons fully recovered from the disease. Such carriers become a serious menace to all with whom they may come in contact.

Morbid Anatomy.—A catarrhal condition exists throughout the large and small intestines. There is hyperplasia of Peyer's patches, which become infiltrated, hardened, and elevated above the mucous membrane. The solitary glands may project into the in-

PLATE VI

Ileum; typhoid fever (early stage): Peyer's patches and solitary follicles greatly swollen; superficial ulceration (Nicholls in "American Textbook of Pathology").

testines. The swollen follicles may undergo resolution or the process may go on to necrosis and sloughing. This is due in part to a choking and obliteration of the blood-vessels by the infiltration, and in part to the direct action of the bacilli upon the cells. Following and dependent upon the sloughing there occurs ulceration. The necrotic tissue gradually separates, beginning at the periphery of the gland, finally becoming detached and leaving ulcers of varying sizes and depths. Upon the separation of the slough, cicatrization begins. The ulcers diminish in size, the floor becoming covered with a layer of delicate granulations. The mucosa gradually extends in from the edge, and a new growth of epithelium is formed. The mesenteric glands are infiltrated, enlarged, and softened, but seldom suppurate. The spleen is enlarged and softened, and parenchymatous degeneration may occur in all the tissues of the body—kidneys, liver, heart, blood-vessels, nervous system, and bone-marrow.

Morbid Physiology.—In addition to interference with the function of the intestines by the local manifestations of the disease, the toxin produces widespread disturbances in other organs. Changes occur in the blood, with an increase of the agglutinins, giving rise to the Widal reaction, with, finally, the establishment of immunity. The fever, apathy, delirium, and the various parenchymatous degenerations are doubtless due to the toxin.

ASIATIC CHOLERA

Definition.—An acute infectious disease caused by the Cholera spirillum, characterized by violent purging and rapid collapse.

Etiology.—The specific cause of this disease is the Cholera spirillum. Infection occurs in the intestine, as in typhoid fever, the source of infection being food or drink contaminated with the excretions of cholera patients. That predisposing causes exist is evidenced by the frequent presence of virulent cholera germs in the stools of healthy individuals. What the predisposing factors may be we are as yet unable to say, though depressing emotions, fear, and debility may have something to do with an increased susceptibility.

Morbid Anatomy.—The peritoneum is sticky and the intestines congested and shrunken. Peyer's glands and Brunner's glands are enlarged. The mucosa is swollen and congested. The germs are found in the intestinal contents and mucous membrane. There is more or less fatty degeneration of the liver and cloudy swelling and extensive coagulation necrosis of the kidneys.

Morbid Physiology.—The profound disturbances of function which occur in this disease are due to the toxin of the germ. There are vomiting and diarrhea. Secretion of the urine and saliva are arrested and the blood becomes thick, due to the rapid extraction of water from the body in the watery stools.

TUBERCULOSIS

Definition.—An infective disease caused by the Bacillus tuberculosis. So termed because of the formation in its lesions of small nodular bodies called tubercles.

Etiology.—There is perhaps no disease to which the animal kingdom is more universally susceptible. It is transmitted by means of the secretions of susceptible animals. Cattle, hogs, and man are the most susceptible; rabbits and guinea-pigs less so; as are also cats and dogs, which are, however, sometimes infected by tuberculous masters. Monkeys appear to be immune in the wild state, but exceedingly susceptible in captivity, bearing out the fact that tuberculosis is a house-bred disease.

Heredity was formerly considered an important predisposing cause, it being thought than an increased susceptibility was transmitted from parent to offspring. It is probable that this is greatly overestimated, and that, indeed, in case of parents who have recovered from tuberculous infection a certain degree of immunity or increased resistance to infection is transmitted to the offspring. The most important predisposing causes are overwork, underfeeding, and poorly ventilated living quarters. There is perhaps no disease in which the susceptibility is so increased by bad living, debilitating diseases, as measles, whooping-cough, pneumonia, grip, etc.

The modes of infection are inhalation, ingestion (in

tuberculous milk), direct inoculation through wounds of the skin, or through the genital tract. Direct transmission to the fetus *in utero* occurs, but is rare. The transmission from one member of a family to another is frequent.

Morbid Anatomy.—No organ of the body is free from the manifestations of this disease. The order of frequency in which the organs are affected in this disease are as follows: lungs, lymph-glands, bones and joints, intestines, peritoneum, kidneys, brain, spleen, liver, and generative organs. Wherever the infection is located it is characterized by the formation of tubercles. The evolution of a tubercle is thus described by Baumgarten:

(1) There is a rapid multiplication of the tubercle bacilli, which is accompanied by their dissemination in the surrounding tissues, partly by growth and partly by the lymph-current.

(2) Multiplication of the fixed cells, especially those of the connective tissue and the endothelium of the capillaries, and the gradual production from them of rounded cuboid or polygonal bodies with vesicular nuclei, the epithelioid cells, inside some of which bacilli are seen.

(3) From the vessels of the infected focus leukocytes (chiefly polynuclear) migrate in numbers and accumulate about the focus of infection. They do not long survive, however, and many undergo destruction. Later, as the little tubercles grow, the leukocytes found are of

PLATE VII

Tuberculosis of the lung: the upper lobe shows advanced cheesy consolidation with cavity formation, bronchiectasis, and fibroid changes; the lower lobe retains its spongy texture, but is occupied by numerous miliary tubercles (McFarland).

the mononuclear variety, which do not undergo the rapid degeneration of the polynuclears.

(4) A reticulum of fibers is formed by the fibrillation and rarefaction of the connective-tissue matrix. This is most apparent, as a rule, at the margin of the growth.

(5) In some tubercles giant cells are formed by increase in the protoplasm and in the nuclei of the individual cells, or possibly by the fusion of several cells.

Once formed the tubercle may undergo—

Caseation.—At the center of the tubercle the cells under the action of the bacilli and their toxins undergo coagulation necrosis and are converted into a structureless mass. The process extends until the entire tubercle is converted into a cheesy, homogeneous mass, in which the bacilli are still active, after which it may undergo softening, encapsulation, or calcification.

Instead of caseation, which must be looked upon as degenerative and dangerous, the tubercle may undergo—

Sclerosis.—With the destruction of the cells at the center of the tubercle there may occur fibroid transformation at the periphery, the tubercle being converted into a firm resistant mass. It is in this manner that healing occurs.

By the fusion of softened caseous tubercles, cavities are formed which are sometimes termed cold abscesses, because of the absence of true pus in their contents.

Morbid Physiology.—In addition to the disturbances of function which the tuberculous infection causes at

the site of infection, toxins are formed which cause constitutional symptoms of varying intensity. There is anemia, wasting, afternoon rise of temperature, and more or less weakness. The nature of the toxic products are not well understood. The well-known reaction to tuberculin in the presence of tuberculous infection and absence of reaction where infection does not exist, would indicate a process differing somewhat from the ordinary toxin production of toxic infections.

LEPROSY

Definition.—A chronic infectious disease caused by the Bacillus lepræ. Characterized by the formation of tuberculous nodules in the skin and mucous membranes, or by trophic changes in the nerves, or by both together.

Etiology.—Of the mode of infection little is known. Some particular susceptibility must be necessary for infection to occur, because, with a single exception, attempts at direct inoculation have failed, while physicians and nurses who care for lepers rarely ever contract the disease. Heredity is supposed to play a part, yet no case is on record of leprosy in the newborn.

Morbid Anatomy.—In the tuberculous form, nodules composed of granulomatous tissue occur on the skin of the face, hands, and forearms, less frequently upon other parts of the body. Between the nodules are sometimes seen areas of ulceration and cicatrization. On

the face this process produces a peculiar appearance termed facies leontina. The mucous membranes may be similarly affected and blindness may occur from involvement of the conjunctiva and cornea, or loss of voice and suffocation from involvement of the larynx. Ulcerations may lead to the loss of toes or fingers. In the anesthetic form there is almost entire absence of the deformities seen in the tuberculous variety of the disease. There may, however, be in this form maculæ and pemphigus-like bullæ of the skin which may ulcerate, thus leading to deformity and contractions or loss of fingers and toes.

Morbid Physiology.—The alterations of function in this disease are entirely local, as there seems to be no toxemia present. Secondary lesions may occur in internal organs—liver, spleen, testes, lungs, etc.—which are similar to the skin lesions. The anesthetic variety lays the parts liable to various injuries from trauma, freezing, burns, etc., because of the loss of sensation.

PLAGUE

Definition.—An acute infectious disease caused by the Bacillus pestis, characterized by inflammation of the lymphatic glands, pneumonia, and hemorrhages.

Etiology.—Filth, squalor, and poverty undoubtedly contribute to the existence and spread of the disease. Infection, especially in the pneumonic type of the disease, may occur by direct dissemination of the germ by in-

fected individuals. Inoculation of cutaneous wounds may also occur, though the bacillus is short lived outside the body and rapidly disappears from water, soil, and air. The most important mode of infection is by inoculation by the bite of the rat flea. Rats, ground squirrels, mice, guinea-pigs, and monkeys are very susceptible to the disease, and practically every outbreak of the disease among human beings is coincident with an epidemic among rats. If the rats are free of fleas close contact of healthy with infected animals does not infect healthy animals, while the mere transference of fleas from infected animals to healthy ones without any association of healthy with infected animals is sufficient to cause an outbreak of the disease among the healthy. It would seem that the pneumonic type is acquired by inhalation of infected material, while the bubonic form is transferred from rats to man by the flea. While rat fleas do not normally attack man, yet upon the death of their normal host they leave the dead body in search of warmth and nourishment, and will then take up their abode temporarily upon the bodies of human beings.

Morbid Anatomy.—There is swelling and inflammation of the lymphatic glands, which tend to suppurate. The inflammation sometimes extends to the adjacent tissues with extravasations of blood. The inguinal glands are most constantly affected, though those of the axilla, neck, and mediastinum may also be affected.

The spleen and intestinal follicles are enlarged. Parenchymatous degeneration of the heart, liver, and kidneys may be found. Ecchymosis and petechiæ and carbuncles of the skin are frequent. In the pneumonic form inflammation of the lungs resembling pneumococcus infection takes place.

Morbid Physiology.—While there is considerable question regarding the character of the toxin formed by this microbe, the existence of such toxin is evidenced by the profound systemic disturbances (chills, fever, approaching 108° F. at times, delirium, stupor, and coma). The heart's action is feeble and rapid, and collapse may take place.

TETANUS

Definition.—An acute infectious disease caused by the Bacillus tetani, characterized by more or less persistent tonic spasms of the voluntary muscles, particularly those of the jaw.

Etiology.—The bacillus is found in great numbers in cultivated soil, street dust, horse manure, and stable detritus. Infection would, therefore, be expected to be a frequent occurrence. That infection is a relatively rare occurrence is due to the specific limitations to the growth and development of the germ.

Being a pure anaërobe, the germ must be protected from oxygen for its growth and development, and infection can, therefore, occur only in punctured or deep-seated wounds. There seems also to be a considerable

resistance to the development of the germs, so that pure cultures freed from toxin and injected into animals do not develop. If, however, they are accompanied by saprophytic germs, chemicals, or other material which may cause a lowered vitality of the surrounding tissues, development and toxin formation takes place. So we find wounds into which foreign material has been carried, as wads in blank-cartridge wounds, pieces of clothing, dust, etc., are particularly prone to become the seat of tetanus infection. The uterus (following delivery) and the umbilicus of the newborn furnish fertile fields for infection.

Morbid Anatomy.—There are very few anatomic changes present in this disease. Some congestion of the membranes of the brain and cord are seen, and recently some structural alterations of the ganglionic cells of the cord have been described.

Morbid Physiology.—The bacilli remain localized and cause little or no disturbance. All the symptoms are caused by the toxin, which reaches the brain and cord by way of the axis-cylinders of the nerve-trunks and not by way of the blood- and lymph-channels. The toxin has a peculiar affinity for the cells of the central nervous system, and is seemingly harmless to other tissues. Its effect upon the nervous system is similar to strychnin, causing violent spasms of the voluntary muscles. It is eliminated by the urine, which is highly toxic. An antitoxin is elaborated in the blood of infected indi-

viduals, but seems incapable of separating the toxin from the nerve-tissue once it has been united with it. Antitoxin treatment, therefore, to be of value must be administered before the nervous symptoms denote the union of toxin with the cells of the nerve-tissue.

GLANDERS

Definition.—An infectious disease caused by the Bacillus mallei, occurring usually in animals, occasionally in man, and characterized by enlargement of the lymphatic glands, especially of the parotid and submaxillary chains, with catarrhal inflammation of the nasal and respiratory mucous membranes.

Etiology.—The specific cause is infection with the Bacillus mallei, predisposing causes being occupations which bring man in contact with horses. Veterinarians, coachmen, teamsters, stablemen, and stockmen are practically the only ones who have the disease.

Morbid Anatomy.—The histologic changes resemble those of pyemia. Peculiar bloody abscesses and ulcers occur over the surface of the body. In the skin, mucous membranes, lungs, liver, brain, and spleen are found nodules of varying size, from a pin-point to that of a walnut. The nodules are found to be made up of necrotic or caseous material in the center surrounded by epithelioid cells, leukocytes, and small round cells. Lymph-glands near the nodules are infiltrated and enlarged.

Morbid Physiology.—There are symptoms referable to a toxin, as fever, headache, and prostration. Painful, red and swollen joints, profuse and fetid expectoration.

ANTHRAX

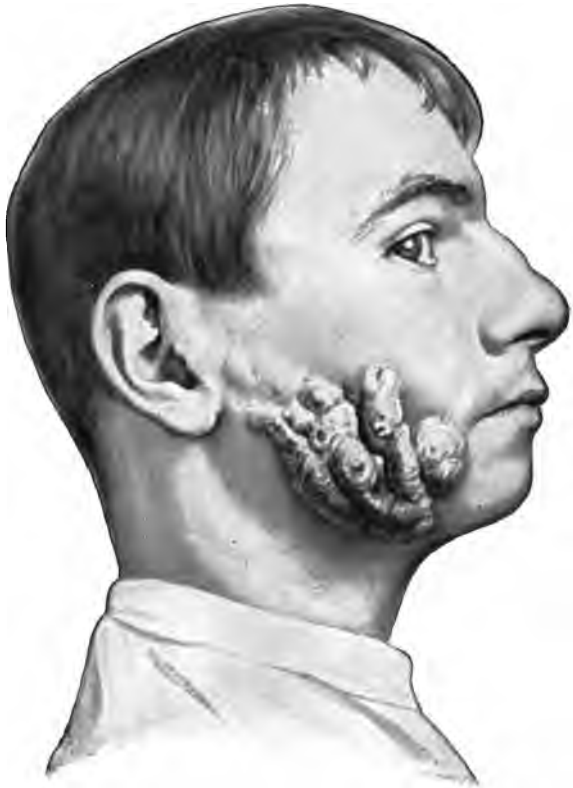
Definition.—An acute infectious disease caused by the anthrax bacillus, occurring usually in animals, but occasionally in man. Characterized by hard edema or ulcers at the point of inoculation and symptoms of collapse.

Etiology.—The exciting cause is the bacillus of anthrax which, in cattle and sheep, gains entrance through the alimentary canal. In man the infection occurs from handling cattle or sheep or their products, as wool, hides, hair, etc., and takes place by direct inoculation through the skin, by inhalation through the respiratory tract, and by ingestion through the elementary tract.

Morbid Anatomy.—The most common form of anthrax in man is due to skin infection, and takes the form of a localized abscess or pustule termed malignant pustule. This may heal or progress to general septicemia. The pulmonary form, or wool-sorters' disease, gives rise to inflammation of the lungs resembling pneumonia. Septicemia may follow. Where septicemia occurs, the blood is found teeming with the germs, which may even clog the capillaries.

Morbid Physiology.—The influence of this infection

PLATE VIII



Actinomycosis of the cheek (Illich).

upon the physiologic processes is not well understood. No toxin has been demonstrated, though an attack confers immunity, and the symptoms of the intestinal form—diarrhea, vomiting, fever, and rapid pulse—resemble a toxemia. In view of the fact that immunity may be produced by vaccination, both with attenuated and dead cultures, it would seem that the immunity was a result of phagocytosis. The opsonic index is high in immune animals and low in susceptible ones, which would also support the phagocytic theory of the immunity.

ACTINOMYCOSIS

Definition.—A chronic infectious disease of cattle, occurring occasionally in man, caused by Actinomyces bovis and characterized by the formation of lumpy tumors.

Etiology.—The disease is due to a peculiar vegetable organism termed the ray fungus. It occurs chiefly in cattle, but occasionally in man, the horse, pig, sheep, dog, cat, and elephant. The mode of infection is still in question, instances occurring in individuals having no association with cattle. Nor has there been any observation of instances of direct contagion among cattle. Because of the frequency of infection in the jaw and about the throat it is supposed to occur through carious teeth.

Morbid Anatomy.—This organism produces a granulation tumor consisting of proliferating connective-tissue

cells and some epithelioid or giant cells. Suppuration of the growth soon takes place and the ray fungus is found in the pus.

Morbid Physiology.—The functional disturbances are due almost entirely to the local process or the septic complications which may arise. There are no toxins formed. Generalization of the infection may occur in man, and emboli may cause death.

INFLUENZA

Definition.—An epidemic disease caused by the Bacillus influenzæ, characterized by fever, depression, muscular pains, and acute catarrhal inflammation of the nose, larynx, and bronchi.

Etiology.—The disease is extremely contagious, though the modes of infection are not well understood. Doubtless the direct transference of the infection from one individual to another is the usual manner in which it takes place.

Morbid Anatomy.—There are no specific lesions in influenza. The mucous membranes of the air-passages are congested and swollen. The bacilli have been found in the brain in cerebral influenza, and in the intestines between the epithelial cells and in the basement-membrane.

Morbid Physiology.—But little is known of the cause of the constitutional disturbances in this disease. They are characteristic of a toxemia, but a toxin has

not as yet been isolated. Immunity is not established by an attack; in fact, increased susceptibility seems to follow.

SYPHILIS

Definition.—A specific infectious disease of slow evolution, caused by the Treponema pallidum.

Etiology.—The cause of this disease has at last been definitely proved to be the Treponema pallidum by the inoculation of apes, which seem to be the only animal besides man which is susceptible to the infection. The infection occurs through minute abrasions of the skin and mucous membranes, and is usually transmitted by sexual intercourse. Innocent infection frequently occurs in nurses and physicians from examining and handling syphilitic patients, and in others through kissing, the use of drinking vessels, etc.

Hereditary transmission is frequent, this being one of the few diseases in which the direct transmission of the disease from parent to offspring may occur. The inheritance may come from either parent. A remarkable fact concerning inherited syphilis is that referred to as Colles' law, which is stated as follows: If a syphilitic child be born of a healthy mother, the child cannot infect such mother, though if it suckle a healthy wet-nurse the nurse will become infected. The mother doubtless receives immunity by way of the placenta without being herself infected.

Morbid Anatomy.—The pathologic manifestations of

this disease are divided into three stages: the primary, secondary, and tertiary.

Primary Lesion.—In the primary stage there occurs at the site of infection an initial lesion termed chancre. This appears as a small papule or vesicle which is reddened and inflamed. This soon becomes eroded and surrounded by a zone of infiltration of peculiar hardness, termed induration. This consists, histologically, of a diffuse infiltration of round cells, large epithelioid cells, and giant cells. Changes occur in the small arteries and veins, leading to an acute obliterative endarteritis which causes the peculiar stony induration. The neighboring lymphatic glands undergo hyperplasia and become indurated.

Secondary Lesions.—After a variable length of time, from three weeks to several months, the secondary manifestations of the disease appear. These include swelling and induration of the superficial lymphatic glands. Various eruptions—macular, papular, and scaly—make their appearance upon the skin. On the mucous membrane occur condylomata or mucous patches, somewhat elevated patches with superficial ulceration or erosion.

Tertiary Lesions.—The most distinctive lesions of this stage are circumscribed tumors, known as gummata, various skin lesions, ulcers, etc., and a peculiar type of arteritis.

Gummata are nodular masses varying in size from

small tubercles to masses the size of an orange or larger, occurring in bones, periosteum, muscle, skin, brain, lungs, liver, kidneys, heart, testes, and adrenals. These masses are composed largely of round cells from the blood-vessels and various proliferated connective-tissue cells of spindle shape or irregular forms. Epithelioid cells are few in number. There are various changes in the vessel walls and new formation of blood-vessels. Necrosis may occur at the center of gummata, and fatty or myxomatous degeneration is common. Atheroma of the arteries may lead to softening of the brain.

Morbid Physiology.—It is probable that the physiologic disturbances in this disease are due to the germ itself, which is recovered from all the lesions of the disease rather than from a specific toxin. Antibodies are found in the blood of infected individuals, and this fact is taken advantage of in the Wassermann or deviation of complement test. All efforts to establish either active or passive immunity have thus far failed, though Ehrlich has succeeded in ridding the system of the disease by injections of an arsenic preparation termed salvarsan or "606."

RELAPSING FEVER

Definition.—A specific infectious disease, caused by the Spirochæta obermeieri, characterized by recurring paroxysms of fever and separated afebrile periods.

Etiology.—Overcrowding, deficient food, squalor, and

filth seem to be conditions favorable to infection with this germ. Just how the infection occurs is not known, but it is suspected that bed-bugs or fleas may be instrumental in its transference.

Morbid Anatomy.—There are no characteristic anatomic alterations in this disease. Ecchymoses of the skin occur, and there have been found enlargement of the spleen, cloudy swelling of the heart, liver, and kidneys, and infarcts of the kidney and spleen, also changes in the bone-marrow.

Morbid Physiology.—No toxins have been demonstrated in this disease, but antibodies for the germs are developed during each paroxysm of fever that rapidly destroy the germs, which are then taken up by the phagocytes. Some, however, appear to withstand the effects of the antibodies and develop and multiply after an interval, either because of the partial disappearance of the antibodies or to an immunity of the surviving germs. When growth and development of the germs begin again, another paroxysm of fever occurs, which is ended as before by the development of antibodies and phagocytosis. The blood becomes finally so charged with antibodies that further growth of the germs is impossible, and recovery occurs, with immunity to further infection. The blood of such immune animals confers immunity on animals injected with it, and is also curative when infection has already occurred.

MALTA FEVER

Definition.—An endemic infectious disease due to the Micrococcus melitensis, characterized by irregular fever, sweats, arthritis, and enlarged spleen.

Etiology.—While it is believed that this infection may be transmitted by mosquito bites, the usual mode of infection is the drinking of the milk of goats which are infected. The milk abounds with the germs, and monkeys have been infected with milk containing the organism.

Morbid Anatomy.—There are no characteristic anatomic changes in this disease.

CHAPTER XXIII

DISEASES WHOSE MICROBIC CAUSE HAS NOT BEEN ISOLATED

THERE yet remain a number of diseases for consideration which are most certainly of microbic origin. The causative germs, however, have not been isolated and subjected to Koch's rules. The list of such diseases is growing shorter every year.

HYDROPHOBIA

Definition.—An infectious disease communicated by the bite of an animal and characterized by severe nervous disturbances and spasms, especially of the muscles of respiration and deglutition.

Etiology.—This is probably due to a specific microorganism which has not yet been isolated. All mammals are susceptible to the disease. The mode of infection is probably always through the bite of an infected animal, usually the dog, though cats, wolves, horses, and cattle may convey the disease.

Morbid Anatomy.—There is congestion of the cord and brain, as in tetanus, and some exudation in the perivascular tissue. Congestion of other organs may occur, as of the gastro-intestinal tract, respiratory system, and kidneys. The only characteristic feature is the presence in the large nerve-cells of the central nervous sys-

tem of certain peculiar bodies termed Negri bodies, after Negri, the investigator who first observed them. The presence of these bodies is considered pathognomonic of the disease. Whether these bodies are micro-organisms or products of the nerve-cells has not yet been determined.

Morbid Physiology.—The alterations of function in this disease resemble very closely those of tetanus, The spasms of the muscles of deglutition are characteristic. They are excited by attempts at swallowing or even the thoughts of swallowing, being provoked by the sight of water. It is from this peculiarity that the desease derives its name. The virus is found in the spinal cord and brain and is always present in the saliva. It makes its way from the point of infection to the brain and cord by way of the nerve-trunks, as in tetanus.

Yellow Fever

Definition.—A fever of tropical and subtropical countries, characterized by jaundice, albuminuria, and a tendency to hemorrhages of the stomach.

Etiology.—The micro-organism which causes this disease has not been isolated, but is known to inhabit the blood of infected patients, as the disease has been produced by injecting the blood of those infected into healthy individuals. The infection is transmitted from individual to individual by the bite of certain species of mosquito. This has been proved to be the only

method of transmission. Members of the Yellow Fever Commission of the United States Army slept for weeks on the bedding of yellow fever patients, slept with the patients, nursed them, and subjected themselves to every possible chance, but did not take the disease while mosquitos were excluded. Mosquitos were allowed to bite patients with the disease and afterward healthy individuals, and the disease followed, Dr. Lazear dying from an attack. Colonel Gorgas by exterminating mosquitos stamped out yellow fever in Havana.

Morbid Anatomy.—The skin is jaundiced and hemorrhages occur from the skin and mucous membranes, especially the mucous membrane of the stomach, where it gives rise to the distinctive black vomit of the disease. The lymphatic glands are enlarged and there is fatty degeneration and areas of necrosis in the liver. The kidneys show diffuse nephritis.

Morbid Physiology.—The fever, profound prostration, and the serious injury to the liver and other internal organs would indicate the presence of a toxin in this disease, but none has been isolated. Immunity is established by an attack. This, however, may be a germicidal rather than a toxic immunity.

MEASLES

Definition.—An acute contagious disease, characterized by catarrhal inflammation of the upper air-passages and a specific eruption of the skin.

Etiology.—The disease is transmitted by contact, by a third person, by toys, books, clothing, etc. The cause is unknown, as is also the nature of the contagion.

Morbid Anatomy.—There are no characteristic anatomic changes. The lymphatic glands are enlarged. The eruptive areas of the skin show some leukocytic infiltration.

Morbid Physiology.—There are no specific alterations of function. Fever and catarrhal disturbances of the mucous membranes are the prominent disturbances.

Scarlet Fever

Definition.—An acute infectious disease characterized by a scarlet eruption, sore throat, and high fever.

Etiology.—The exciting cause is unknown. Age is a predisposing cause. It occurs most frequently from the second to the tenth year; 90 per cent. of cases occur before the tenth year. There is a great variation of personal susceptibility. Some individuals are apparently immune. The infecting agent is very resistant, and infection is often conveyed by clothing, books, toys, carpets, etc., months after the occurrence of the disease.

Morbid Anatomy.—There are no specific pathologic changes. The changes in the throat are those of any simple inflammation. The internal alterations are those due to fever and to pus organisms, which seem to always complicate the disease. The spleen, liver, and other

organs sometimes show necrotic foci. The most constant and typic complicating lesion is inflammation of the kidneys, scarlatinal nephritis. Streptococci are constantly present in great numbers, and by some are considered to be the cause of the disease. Certain it is that they are the cause of many of the complications, as otitis, mastoiditis, etc.

Morbid Physiology.—The fever, prostration, and general disturbances are simply characteristic of inflammation. An attack confers immunity, but how it does so is not known.

PAROTITIS (MUMPS)

Definition.—An acute infectious and contagious disease, characterized by swelling of the parotid glands and a liability to orchitis.

Etiology.—The specific cause is unknown. The disease occurs most frequently in childhood and early adult life.

Morbid Anatomy.—There is inflammation of one or both parotid glands, with catarrhal condition of the ducts. Inflammation of one or both testicles may occur and is sometimes followed by atrophy. The mammary glands and ovaries are less frequently involved.

Morbid Physiology.—No specific alterations occur.

PERTUSSIS (WHOOPING-COUGH)

Definition.—An acute specific affection, occurring usually in children and characterized by a peculiar convulsive cough, ending with an inspiratory whoop.

Etiology.—The specific cause has not been isolated. It is extremely contagious and is usually transferred directly from one individual to another. One attack usually confers immunity.

Morbid Anatomy.—The disease has no special anatomic changes, but enlargement of the tracheal and bronchial tubes is commonly present.

Morbid Physiology.—There are no specific disturbances. There is increased leukocytosis, and sugar and albumin may appear in the urine.

Typhus Fever

Definition.—A contagious fever, characterized by high temperature, great prostration, and a petechial eruption.

Etiology.—The specific germ is as yet unknown, but the contagion is probably conveyed by the breath and secretions of the skin. Recent investigations indicate the presence of an insect carrier. Filth, squalor, overcrowding, poor ventilation, and bad food are doubtless predisposing causes.

Morbid Anatomy.—Changes characteristic of high fever occur, as enlargement of the spleen and swelling of the kidneys. The liver is enlarged and softened, and granular degeneration of the muscles, especially of the heart, is frequent. A petechial rash of the skin is present.

Morbid Physiology.—The disturbances of function are those of fever.

CHAPTER XXIV

DISEASES DUE TO ANIMAL PARASITES

Diseases Due to Protozoa

AMEBIC DYSENTERY

Definition.—An acute or chronic colitis due to the Amœba dysenteriæ.

Etiology.—The disease usually occurs in tropical climates. Nothing is known of the life-history of the ameba outside the body, but infection probably occurs through drinking-water or raw foods. Amebæ are found in the stools of healthy individuals, but whether there exists an immunity in some persons or whether there are pathogenic and non-pathogenic varieties of the parasite is not at present known.

Morbid Anatomy.—Ulcerations of the walls of the large bowel are always present in this disease. Abscess of the liver frequently accompanies the intestinal process. The disease progresses by a gradual infiltration of the connective-tissue layers of the intestines. The infiltration is composed of proliferative connective-tissue cells. Amebæ are found in the ulcers and the surrounding lymphatic spaces.

Morbid Physiology.—There are general functional disturbances. The condition of the bowel causes diarrhea and consequent weakness.

TRYPANOSOMIASIS (SLEEPING-SICKNESS)

Definition.—A chronic disorder due to the Trypanosoma gambiense, characterized by fever, lassitude, weakness, and often protracted lethargy.

Etiology.—This disease is prevalent in West Africa and is due to the trypanosome. Infection occurs by the bite of a fly, the Glossina palpalis. This fly lives on the bushes and weeds along the shores of streams and lakes.

Morbid Anatomy.—The parasite is found in the cerebrospinal fluid and blood. In the early stage of the disease the lymphatic glands are enlarged and the parasite is found in them.

Morbid Physiology.—The manner in which the parasite produces its characteristic disturbances—fever, rapid pulse, dulling of the mind, tremors, and, finally, subnormal temperature and coma—has not yet been determined.

MALARIAL FEVER (AGUE)

Definition.—An infectious disease caused by the Plasmodium malariæ, characterized by periodic occurrences of chill, fever, and sweating.

Etiology.—The disease is contracted through the bite

of the Anopheles mosquito, in whose body the parasite passes through its sexual cycle of development. In the red blood-corpuscles of the warm-blooded host an asexual cycle of development takes place, each parasite developing into fifteen to twenty spores or daughter-cells, the chills and fever characteristic of the disease being coincident with the maturing and scattering into the blood of these daughter-cells. After several generations, sexual forms are developed, which, however, are incapable of fertilization in the blood. When the blood enters the stomach of the mosquito the male elements fertilize the female elements, which enter the walls of the stomach and give birth to a swarm of the asexual form of the parasite. Numbers of these gather in the veneno-salivary glands and are injected into man when the mosquito feeds upon him.

Morbid Anatomy.—The morbid alterations are the result of the disintegration of the red blood-corpuscles, the accumulation of pigment thus formed, and possibly to the development of a toxin. The spleen is enlarged and there may be parenchymatous degeneration of the kidneys. The liver is enlarged and turbid. Anemia rapidly develops, with a lowering of the hemoglobin.

Morbid Physiology.—The chill, fever, and sweating are the result of the changes in the blood, which takes place with the maturing of the parasites within the red corpuscles, which are rapidly destroyed thereby.

Diseases Caused by Cestodes

Tapeworms

Tapeworms have two states—the larval state, which is found in one species of animal, and the adult state, occurring in another species.

Tænia Solium, or Pork Tapeworm.—This is composed of a small head armed with suckers and a double row of hooklets, whereby it attaches itself to the intestines, a slender neck, and numerous segments which compose the body. Each segment contains male and female elements. At maturity the segments contain thousands of ripe ova. The segments are continually discharged with the bowel movements. Each ovum contains an embryo with six hooklets. To develop further, the ovum must be taken into the stomach of the pig or man. There the shell is digested, and the embryo set free, passes through the stomach wall and becomes encysted in various organs, as the muscles, brain, liver, or eye, where they develop into larvæ or cysticerci. When the flesh containing the cysticerci is eaten by man or certain other animals the cyst is dissolved, the parasite fastens itself to the mucous membrane of the intestine, and develops into the adult worm, with segments and ova as before. While either the larval or the adult stage of this tapeworm may occur in man, it is usually the adult type to whom man is host.

Morbid Anatomy.—No anatomic changes occur.

Morbid Physiology.—Practically the only disturbance

caused by this parasite is due to local irritation—diarrhea, pain, and nausea. Occasionally chorea and convulsions occur. It has been thought that products of this parasite have a hemolytic action, thus causing the anemia.

Tænia Saginata.—This worm passes the larval state in cattle and the adult state only in man. It differs only in size and shape from the solium, and the disturbances caused are the same.

Cysticercus Cellulosæ.—When the ripe ova of Tænia solium are accidentally swallowed by man he becomes the host for the larval form of the parasite, a much more serious matter than harboring the adult parasite. The results depend upon the number of the ova swallowed and upon the organs upon which they locate. In the muscles they cause soreness and pain; in the eye, possibly blindness; in the brain, various undefined nervous manifestations, all due to the irritation and pressure of their growth.

ECHINOCOCCUS DISEASE

This parasite occurs in the larval state in man, the adult stage being passed in the dog, wolf, and fox. The eggs having been swallowed, the embryo parasite is freed in the stomach, penetrates the mucous membrane, and is carried by the blood to the liver, spleen, kidneys, or brain, where it develops an echinococcus cyst, a sac containing fluid and the parasite. The cyst may

reach enormous size, or the parasite may die and the cyst shrivel and disappear.

Morbid Anatomy.—The increasing size of the cyst causes destruction of surrounding tissue and pressure-atrophy. In the brain, death may occur early with pressure symptoms.

Morbid Physiology.—This depends upon the location of the cyst and its size.

Diseases Caused by Nematodes or Round-worms

Ascaris Lumbricoides

This is one of the most common small parasites affecting man. The worm develops in the small intestine after swallowing of the eggs in food or drink. The worm resembles in appearance the earthworm or common angleworm. While it inhabits the small intestine principally, it sometimes migrates to other parts, as the gall-ducts, the stomach, the esophagus, or even the larynx. They give rise to few symptoms aside from intestinal irritation. Large masses have caused intestinal obstruction.

Oxyuris Vermicularis

This parasite is termed the thread-worm or seat-worm. It inhabits the colon or rectum commonly in children. It may migrate to the vagina. It causes intense itching and irritation.

TRICHINA SPIRALIS

Trichina occurs in both the larval and adult form in man and the lower animals. Infection occurs from eating improperly cooked pork. The larvæ are set free, develop into adults in the intestines, where they discharge embryos. Some of the embryos die or escape by the feces, while others penetrate the intestinal wall, and are either carried by the blood or lymph-stream or by their own migrations to the muscles, where they become encysted. When the migration begins, symptoms of intestinal irritation, with fever, vomiting, and perhaps collapse occur, followed by excruciating pain in the muscles resembling rheumatism, the gravity of the disturbance depending upon the number of the parasites developed.

ANKYLOSTOMA DUODENALE (HOOK-WORM)

This worm is so called from the head being armed with six sharp hook-like teeth, whereby it fastens itself to the wall of the small intestine. The parasite causes intense anemia and debility. It is thought that a poison is secreted by the worm, which causes the profound blood changes.

FILARIA SANGUINIS HOMINIS

This is a small worm about the thickness of the diameter of a red blood-corpuscle. Infection occurs through the bite of a mosquito, in whose body occurs one cycle

in its life-history. It is a disease of tropical climates. The embryos may be found in considerable numbers in the blood at night in day workers, or during the day in those who work during the night. The embryos occur in such numbers at times as to block the lymph-channels, producing the conditions known as hematochyluria, elephantiasis, and lymphy scrotum.

Morbid Anatomy.—Opportunities for examining these cases postmortem are rare. In a case examined, the renal and peritoneal lymph-plexuses were enormously distended.

Morbid Physiology.—Chyle and blood are passed with the urine, and the scrotum becomes infiltrated with lymph, which flows freely if the skin be punctured.

INDEX

Books for Nurses

PUBLISHED BY

W. B. SAUNDERS COMPANY

West Washington Square Philadelphia

London: 9, Henrietta Street, Covent Garden

Sanders' Nursing

A NEW WORK

Miss Sanders' new book is undoubtedly the most complete and most practical work on nursing ever published. Everything about every subject with which the nurse should be familiar is detailed in a clean cut, definite way. There is no other nursing book so full of good, practical information—information you need.

Modern Methods in Nursing. By GEORGIANA J. SANDERS, formerly Superintendent of Nurses at Massachusetts General Hospital. 12mo of 881 pages, with 227 illustrations. Cloth, $2.50 net.

Aikens' Home Nurse's Handbook

PRACTICAL

The point about this work is this: It tells you, and *shows* you just how to do those little—but none the less important—things entirely omitted from other nursing books, or at best only incidentally treated. The chapters on "Home Treatments" and "Every-Day Care of the Baby," stand out as particularly practical. Then the "Points to be Remembered"—terse, crisp reminders—is a feature of great value.

Home Nurse's Handbook. By CHARLOTTE A. AIKENS, formerly Director of the Sibley Memorial Hospital, Washington, D.C. 12mo of 276 pages, illustrated. Cloth, $1.50 nei

Stoney's Nursing

NEW (4th) EDITION

Of this work the *American Journal of Nursing* says: "It is the fullest and most complete and may well be recommended as being of great general usefulness. The best chapter is the one on observation of symptoms which is very thorough." There are directions how to *improvise* everything.

Practical Points in Nursing. By EMILY M. A. STONEY, formerly Superintendent of the Training School for Nurses in the Carney Hospital, South Boston, Mass. 12mo, 495 pages, illustrated. Cloth, $1.75 net.

Stoney's Materia Medica

NEW (3d) EDITION

Stoney's Materia Medica was written by a head nurse who knows just what the nurse needs. *American Medicine* says it contains "all the information in regards to drugs that a nurse should possess."

Materia Medica for Nurses. By EMILY M. A. STONEY, formerly Superintendent of the Training School for Nurses in the Carney Hospital, South Boston, Mass. 12mo volume of 300 pages. Cloth, $1.50 net.

Stoney's Surgical Technic

NEW (3d) EDITION

The first part of the book is dovoted to Bacteriology and Antiseptics; the second part to Surgical Technic, Signs of Death, Bandaging, Care of Infants, etc.

Bacteriology and Surgical Technic for Nurses. By EMILY M. A. STONEY. Revised by FREDERIC R. GRIFFITH, M. D., New York. 12mo volume of 311 pages, fully illustrated. Cloth, $1.50 net.

Goodnow's First-Year Nursing

ILLUSTRATED

Miss Goodnow's work deals *entirely* with the *practical* side of first-year nursing work. It is the *application* of text-book knowledge. It tells the nurse *how* to do those things she is called upon to do in her first year in the training school—the *actual ward work.*

First-Year Nursing. By MINNIE GOODNOW, R. N., formerly Superintendent of the Women's Hospital, Denver. 12mo of 328 pages, illustrated. Cloth, $1.50 net.

Aikens' Hospital Management

This is just the work for hospital superintendents, training-school principals, physicians, and all who are actively interested in hospital administration. *The Medical Record* says: "Tells in concise form exactly what a hospital should do and how it should be run, from the scrubwoman up to its financing."

Hospital Management. Arranged and edited by CHARLOTTE A. AIKENS, formerly Director of Sibley Memorial Hospital, Washington, D. C. 12mo of 488 pages, illustrated. Cloth, $3.00 net

Aikens' Primary Studies

NEW (2d) EDITION

Trained Nurse and Hospital Review says: "It is safe to say that any pupil who has mastered even the major portion of this work would be one of the best prepared first year pupils who ever stood for examination."

Primary Studies for Nurses. By CHARLOTTE A. AIKENS, formerly Director of Sibley Memorial Hospital, Washington, D. C. 12mo of 437 pages, illustrated. Cloth, $1.75 net.

Aikens' Training-School Methods and the Head Nurse

This work not only tells how to teach, but also what should be taught the nurse and *how much*. The *Medical Record* says: "This book is original, breezy and healthy."

Hospital Training-School Methods and the Head Nurse. By CHARLOTTE A. AIKENS, formerly Director of Sibley Memorial Hospital, Washington, D. C. 12mo of 267 pages. Cloth, $1.50 net.

Aikens' Clinical Studies

NEW (2d) EDITION

This work for second and third year students is written on the same lines as the author's successful work for primary students. *Dietetic and Hygienic Gazette* says there "is a large amount of practical information in this book."

Clinical Studies for Nurses. By CHARLOTTE A. AIKENS, formerly Director of Sibley Memorial Hospital, Washington, D. C. 12mo of 569 pages, illustrated Cloth, $2.00 net

Bolduan and Grund's Bacteriology

The authors have laid particular emphasis on the immediate application of bacteriology to the art of nursing. It is an *applied bacteriology* in the truest sense. A study of all the ordinary modes of transmission of infection are included.

Applied Bacteriology for Nurses. By CHARLES F. BOLDUAN, M.D., Assistant to the General Medical Officer, and MARIE GRUND, M.D., Bacteriologist, Research Laboratory, Department of Health, City of New York. 12mo of 166 pages, illustrated. Cloth, $1.25 net.

Fiske's The Body

A NEW IDEA

Trained Nurse and Hospital Review says "it is concise, well-written and well illustrated, and should meet with favor in schools for nurses and with the graduate nurse."

Structure and Functions of the Body. By ANNETTE FISKE, A. M., Graduate of the Waltham Training School for Nurses, Massachusetts. 12mo of 221 pages, illustrated. Cloth, $1.25 net

Beck's Reference Handbook

NEW (3d) EDITION

This book contains all the information that a nurse requires to carry out any directions given by the physician. The *Montreal Medical Journal* says it is "cleverly systematized and shows close observation of the sickroom and hospital regime."

A Reference Handbook for Nurses. By AMANDA K. BECK, Graduate of the Illinois Training School for Nurses, Chicago, Ill. 32mo volume of 244 pages. Bound in flexible leather, $1.25 net.

Roberts' Bacteriology & Pathology

This new work is practical in the strictest sense. Written specially for nurses, it confines itself to information that the nurse should know. All unessential matter is excluded. The style is concise and to the point, yet clear and plain. The text is illustrated throughout.

Bacteriology and Pathology for Nurses. By JAY G. ROBERTS, Ph. G., M. D., Oskaloosa, Iowa. 12mo of 206 pages, illustrated. $1.25 net.

DeLee's Obstetrics for Nurses

FOURTH EDITION

Dr. DeLee's book really considers two subjects—obstetrics for nurses and actual obstetric nursing. *Trained Nurse and Hospital Review* says the "book abounds with practical suggestions, and they are given with such clearness that they cannot fail to leave their impress."

Obstetrics for Nurses. By JOSEPH B. DELEE, M. D., Professor of Obstetrics at the Northwestern University Medical School, Chicago. 12mo volume of 508 pages, fully illustrated. Cloth, $2.50 net.

Davis' Obstetric & Gynecologic Nursing

NEW (4th) EDITION

The Trained Nurse and Hospital Review says: "This is one of the most practical and useful books ever presented to the nursing profession." The text is illustrated.

Obstetric and Gynecologic Nursing. By EDWARD P. DAVIS, M. D., Professor of Obstetrics in the Jefferson Medical College, Philadelphia. 12mo volume of 480 pages, illustrated. Buckram, $1.75 net.

Macfarlane's Gynecology for Nurses

JUST READY—NEW (2d) EDITION

Dr. A. M. Seabrook, Woman's Hospital of Philadelphia, says: "It is a most admirable little book, covering in a concise but attractive way the subject from the nurse's standpoint. You certainly keep up to date in all these matters, and are to be complimented upon your progress and enterprise."

A Reference Handbook of Gynecology for Nurses. By CATHARINE MACFARLANE, M. D., Gynecologist to the Woman's Hospital of Philadelphia. 32mo of 156 pages, with 70 illustrations. Flexible leather, $1.25 net.

McKenzie's Exercise in Education and Medicine

Exercise in Education and Medicine. By R. TAIT MCKENZIE, B.A., M.D., Professor of Physical Education, and Director of the Department, University of Pennsylvania. Octavo of 406 pages, with 346 illustrations. Cloth, $3.50 net.

Böhm & Painter's Massage

JUST READY

The methods described are those employed in Hoffa's Clinic —methods that give results. Every step is illustrated, *showing* you the exact direction of the strokings. The pictures are *large.*

Octavo of 91 pages, with 97 illustrations. By MAX BOHM, M. D., Berlin, Germany. Edited by CHARLES F. PAINTER, M. D., Professor of Orthopedic Surgery, Tufts College Medical School, Boston. Cloth, $1.75 net.

Eye, Ear, Nose, and Throat Nursing

Medical Record says: "Every side of the question has been fully taken into consideration."

Nursing in Diseases of the Eye, Ear, Nose and Throat. By the Committee on Nurses of the Manhattan Eye, Ear and Throat Hospital. 12mo of 260 pages, illustrated. Cloth, $1.50 net.

Friedenwald and Ruhrah's Dietetics for Nurses

JUST READY—NEW (3d) EDITION

This work has been prepared to meet the needs of the nurse, both in training school and after graduation. *American Journal of Nursing* says it "is exactly the book for which nurses and others have long and vainly sought."

Dietetics for Nurses. By JULIUS FRIEDENWALD, M. D., Professor of Diseases of the Stomach, and JOHN RUHRAH, M. D., Professor of Diseases of Children, College of Physicians and Surgeons, Baltimore. 12mo volume of 431 pages. Cloth, $1.50 net

Friedenwald & Ruhrah on Diet

FOURTH EDITION

Diet in Health and Disease. By JULIUS FRIEDENWALD, M.D., and JOHN RUHRAH, M.D. Octavo volume of 857 pages. Cloth, $4.00 net.

Galbraith's Personal Hygiene and Physical Training for Women

ILLUSTRATED

Personal Hygiene and Physical Training for Women. By ANNA M. GALBRAITH, M. D., Fellow New York Academy of Medicine. 12mo of 371 pages, illustrated. Cloth, $2.00 net.

Galbraith's Four Epochs of Woman's Life

THE NEW (2d) EDITION

The Four Epochs of Woman's Life. By ANNA M. GALBRAITH, M.D. With an Introductory Note by JOHN H. MUSSER, M. D., University of Pennsylvania. 12mo of 247 pages. Cloth, $1.50 net.

McCombs' Diseases of Children for Nurses

NEW (2d) EDITION

Dr. McCombs' experience in lecturing to nurses has enabled him to emphasize *just those points that nurses most need to know.* *National Hospital Record* says: "We have needed a good book on children's diseases and this volume admirably fills the want." The nurse's side has been written by head nurses, very valuable being the work of Miss Jennie Manly.

Diseases of Children for Nurses. By ROBERT S. MCCOMBS, M. D., Instructor of Nurses at the Children's Hospital of Philadelphia. 12mo of 470 pages, illustrated. Cloth, $2.00 net

Wilson's Obstetric Nursing NEW (2d) EDITION

In Dr. Wilson's work the entire subject is covered from the beginning of pregnancy, its course, signs, labor, its actual accomplishment, the puerperium and care of the infant. *American Journal of Obstetrics* says: "Every page empasizes the nurse's relation to the case."

A Reference Handbook of Obstetric Nursing. By W. REYNOLDS WILSON, M.D., Visiting Physician to the Philadelphia Lying-in Charity. 32mo of 355 pages, illustrated. Flexible leather, $1.25 net

American Pocket Dictionary JUST READY NEW (8th) EDITION

The *Trained Nurse and Hospital Review* says: "We have had many occasions to refer to this dictionary, and in every instance we have found the desired information."

American Pocket Medical Dictionary. Edited by W. A. NEWMAN DORLAND, A. M., M. D., Loyola University, Chicago. Flexible leather, gold edges, $1.00 net; with patent thumb index, $1.25 net.

Lewis' Anatomy and Physiology THIRD EDITION

Nurses Joarnal of Pacific Coast says "it is not in any sense rudimentary, but comprehensive in its treatment of the subjects." The low price makes this book particularly attractive.

Anatomy and Physiology for Nurses. By LEROY LEWIS, M.D., Lecturer on Anatomy and Physiology for Nurses, Lewis Hospital, Bay City, Mich. 12mo of 326 pages, 150 illustrations. Cloth, $1.75 net.

Boyd's State Registration for Nurses

State Registration for Nurses. By LOUIE CROFT BOYD, R. N., Graduate Colorado Training School for Nurses. Price, 50 cents net.

Paul's Materia Medica

NEW (2d) EDITION

A Text-Book of Materia Medica for Nurses. By GEORGE P. PAUL, M.D., Samaritan Hospital, Troy, N. Y. 12mo of 282 pages. Cloth, $1.50 net.

Paul's Fever Nursing

NEW (2d) EDITION

Nursing in the Acute Infectious Fevers. By GEORGE P. PAUL, M.D. 12mo of 246 pages, illustrated. Cloth, $1.00 net.

Hoxie & Laptad's Medicine for Nurses

JUST READY—NEW (2d) EDITION, REWRITTEN

Medicine for Nurses and Housemothers. By GEORGE HOWARD HOXIE, M.D., University of Kansas; and PEARL L. LAPTAD. 12mo of 351 pages, illustrated. Cloth, $1.50 net.

Grafstrom's Mechano-therapy

SECOND EDITION

Mechano-therapy (Massage and Medical Gymnastics). By AXEL V. GRAFSTROM, B.Sc. M.D., 12mo, 200 pages. Cloth, $1.25 net.

Nancrede's Anatomy

NEW (7th) EDITION

Essentials of Anatomy. CHARLES B. G. DENANCREDE, M.D., University of Michigan. 12mo, 400 pages, 180 illustrations. Cloth, $1.00 net.

Morrow's Immediate Care of Injured

Immediate Care of the Injured. By ALBERT S. MORROW, M.D., New York City Home for Aged and Infirm. Octavo of 354 pages, with 242 illustrations. Cloth, $2.50 net. New (2d) Edition

Register's Fever Nursing

A Text Book on Practical Fever Nursing. By EDWARD C. REGISTER, M.D., North Carolina Medical College. Octavo of 350 pages, illustrated. Cloth, $2.50 net.

Pyle's Personal Hygiene

NEW (5th) EDITION

A Manual of Personal Hygiene. Edited by WALTER L. PYLE, M.D. Wills Eye Hospital, Philadelphia. 12mo, 323 pages, illus. $1.50 net.

Morris' Materia Medica

NEW (7th) EDITION

Essentials of Materia Medica, Therapeutics, and Prescription Writing. By HENRY MORRIS, M.D. Revised by W. A. BASTEDO, M.D., Columbia University, N. Y. 12mo of 300 pages, illustrated. Cloth, $1.00 net.

Griffith's Care of the Baby

NEW (5th) EDITION

The Care of the Baby. By J. P. CROZER GRIFFITH, M.D., University of Pennsylvania. 12mo of 455 pages, illustrated. Cloth, $1.50 net.

RETURN TO → Biology Library 0808

LOAN PERIOD 1	2	3
4	5	6

ALL BOOKS MAY BE RECALLED AFTER 7 DAYS

RENEWALS AND RECHARGES MAY BE MADE 4 DAYS PRIOR TO DUE DATE.
LOAN PERIODS ARE 1-MONTH, 3-MONTHS, AND 1-YEAR.
RENEWALS: CALL [redacted]

DUE AS STAMPED BELOW

OCT 20 1991		

UNIVERSITY OF CALIFORNIA, BERKELEY
FORM NO. DD0, 15m, 2/84 BERKELEY, CA 94720