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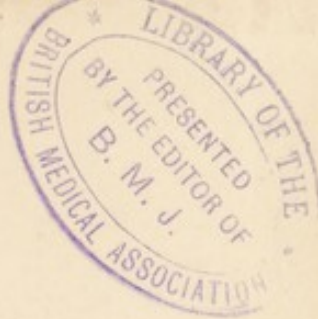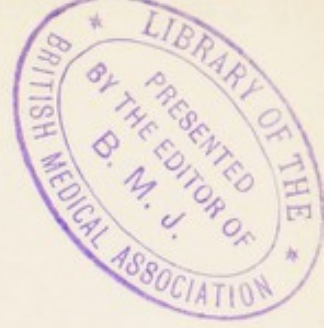
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INFECTIOUS DISEASES
OF INFANCY AND
CHILDHOOD

CLINICAL PEDIATRICS

INFECTIOUS DISEASES OF INFANCY AND CHILDHOOD

BY

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PREFACE

Abraham Jacobi once said that pediatrics was the specialty of the general practitioner. It is not a narrow specialty, for it deals not with a single organ or set of organs but with the entire body.

It is with this view in mind that this set of monographs has been prepared. The present volume, which deals with the communicable diseases of children, is not written for the specialist but for the practicing physician. Theoretical and unproved explanations of the etiology and pathogenesis of some of these disorders have been omitted. The idea is to provide an everyday, useful and dependable book which can be consulted when the occasion arises and the salient facts found without reading several pages of discussion of theories. The main emphasis is placed on practical points, not on theoretical dissertation.

One point needs to be emphasized: A child is not an adult in miniature—a small edition of an adult. The general practitioner who holds this belief and treats his children accordingly makes a very serious mistake. The contrast between the young child and the adult is perhaps not so striking as that of the caterpillar and the butterfly or the tadpole and the frog, but there are mental, physical and physiological differences which are almost as great. Shakespeare recognized these differences when he wrote of the seven ages of man. They must be accepted and understood by a physician if he expects to treat children in an intelligent and sympathetic manner.

Imagine if you can a baby projected to the size of a man and you have a monstrosity with a head one-fourth the size of its body and with the arms and legs out of all proportion. The internal organs show a similar contrast. In the first five years of life the heart nearly quadruples its weight, due to the development of the heart muscles. It is of the utmost importance that this rapidly growing heart be protected from strain and overexertion, and especially from the toxic effects and byproducts of the communicable disease of early childhood. This is one of the reasons why over 2 per cent of all children reaching school age have some defect of the heart muscles or valves of the heart. The brain, for example, has a chemical composition quite different from the adult; its weight in relation to the entire body is 14 per cent, while in an adult it is 2½ per cent. The higher percentage in the child is due to the large proportion of water. The brain cells differ materially from those in the mature brain and the nerve trunks are not connected and can not function properly. In fact, the entire nervous system, including the brain, is in a rudimentary and undeveloped state.

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This is one of the reasons why very slight fever or disease toxins give rise to violent and severe reactions, such as convulsions and delirium. Minor ailments in the child upset the entire organism more completely than in the adult.

A golden rule for all physicians who are called to attend sick children is to treat the child and not necessarily the disease.

The difference between the child and the adult must also be borne in mind when prescribing drugs. The dose is not calculated by reducing the adult dose proportionately. The very great activity of cell life and growth, the more rapid circulation of the lymph and blood streams and the greater excitability of the vasomotor system in the child lead to a more rapid absorption of drugs.

A child, when he reaches school age, enters into the social life of the community and comes into contact with other children. This opens the door for contracting the so-called children's diseases which are discussed in this volume. Diseases caused by microörganisms are called infectious. The process by which they are transmitted is known as infection, and the mode of transmission as contagion. These terms are synonymous for all practical purposes, but the word "communicable" is now in general use to describe all diseases that can be communicated directly or indirectly from one person to another.

The syllabus giving our present knowledge of the nature and methods of control of communicable diseases prepared by a committee of the American Public Health Association and approved by the United States Public Health Service has been added to each chapter. A brief synopsis of the public health law requirements and the duties of the physician attending cases of communicable disease has been included in the discussion of each disease. The statistical tables were prepared from the official records of the New York State Department of Health by Dr. Joseph V. DePorte, Director of the Division of Vital Statistics, and Miss Parkhurst, Research Assistant. The author has received valuable aid and assistance from Mr. Burt Rickards of the Division of Public Health Education of the New York State Department of Health, and Dr. Marion Collins, in the compilation and preparation of this volume. Dr. William E. Lawson, Physician in Charge, Albany Hospital Tuberculosis Sanitarium, with the assistance of Drs. H. Dunham Hunt and John K. Degan wrote the chapter on tuberculosis. Dr. Edward S. Godfrey, Jr., Director of the Division of Communicable Diseases and an epidemologist of international repute, has written an introductory chapter dealing with the responsibility of the attending physician in cases of communicable diseases not alone to the patient but to the community.

HENRY L. K. SHAW.

PUBLISHERS' ANNOUNCEMENT

The publishers take pleasure in presenting to the medical profession the series of monographs of which this volume forms a unit.

The many inquiries which reached them proved, in advance of publication, that the work should be in monographic form and clinical in its presentation.

The series when completed will, they believe, be the most useful for the audience for whom it is written, the general practitioner of medicine, that has been presented in its particular field.

The authors are all men of wide experience and, in the main, teachers. The combination makes the work authoritative and of the utmost service in a field which has been often termed a "therapeutic specialty."

ILLUSTRATIONS

PLATES

INFECTIOUS DISEASES OF INFANCY AND CHILDHOOD

CHAPTER I

INTRODUCTION

EDWARD S. GODFREY, JR.

The phrase "the practicing physician constitutes the first line of defense in the control of communicable disease" has become a banality and yet when a medical practitioner seeks enlightenment of his duties and responsibilities to local and state governments not infrequently he is met by hazy generalizations. He is nearly always reminded of his legal obligation to report to the constituted authorities any communicable disease occurring in his practice and of his obligation to teach his clientele how to avoid the ills that beset mankind. The first of these is often an irksome duty and is apt to be especially so if it is not clear to him just what purpose is served by his fulfilling it; the second is a large order, for all that he can hope to inculcate are a few general principles, giving particular directions only in particular cases.

It is important for all concerned therefore that a physician should have a clear understanding of the principles which guide health authorities and that the advice which he dispenses be based upon sound doctrine. It should be remembered that public health administration as well as medicine is an advancing science and that as knowledge increases rules and regulations are apt to change, to have a sounder reason for their existence and to become less rule-of-thumb.

In the main these changes tend toward simplification, the elimination of useless procedures and restrictions and the substitution of investigation and instruction for the exercise of police power. The passing of terminal fumigation and the "air-tight" domestic quarantine are instances in point. Other time-honored customs are also undergoing a critical scrutiny and it is not improbable that some of them will be modified or discarded as their value is more accurately evaluated. It behooves the practitioner then to keep in touch with these advances, to be open-minded and willing to form his opinion on the facts rather than to retain his prejudices. He can do a great amount

of harm by uninformed criticism of a health department, just as he can do a great amount of good by proper criticism of unsound practices.

The general practitioner is becoming more necessary than he ever has been before in the task of securing further reductions in the morbidity and mortality rates of the communicable diseases. The routes of infection which expose large numbers of people to these diseases are being cut to comparatively negligible proportions. Water supplies are more carefully chosen as to sources and are filtered or chlorinated, or both, to assure the absence of possible infection; milk is now more carefully inspected, and as the rôle of the carrier is better appreciated, a greater and greater proportion of it is being pasteurized. The diseases commonly spread from person to person, however, can be reached by no such thoroughgoing wholesale methods. It is people who must be dealt with, and although we may deal with them in the mass we have to remember that the mass is but a collection of individuals. The average intelligent individual of to-day, while he reads the "health columns," listens to health lectures or radio talks and looks at health movies, usually asks his doctor's opinion before making up his mind as to the truth or reasonableness of what he has heard or read. If there is general professional agreement, public opinion is formed accordingly and this is the great moving force in public health work of to-day in civilized communities.

It is becoming more apparent as time goes on that the attending physician must largely abandon the passive attitude he has been wont to take in the past and assume the aggressive. He must give advice where it is not sought and so far as he can with decency and decorum, urge the value of services he is able to render but of which his patients are unaware. The most important of these services is probably his ability to immunize, actively or passively, against several of the common communicable diseases of childhood.

At this point it may be well to consider briefly some of the more salient features of infection and immunity. Infection, or perhaps one may better say clinical infection, is the result of the overcoming of the bodily defenses by an invading pathogenic microörganism. The fact frequently lost sight of is that there is a quantitative as well as a qualitative aspect to the phenomenon. Although with a few exceptions the factors cannot be measured with precision yet the *amount,* as well as the *degree* of virulence, of the invader is a determinant on the one hand just as is the degree of resistance or immunity on the other.

The virulence of an organism may depend either upon the quantity of toxin it is able to produce or upon the rapidity with which it is able to multiply in the body as well as upon its ability to penetrate the body's defenses. Most bacteria have a special affinity for the cells of certain parts of the body and in some instances produce their characteristic disease only when

they succeed in reaching and in multiplying in such a focus. Thus the meningococcus though a not uncommon inhabitant of the nasopharynx commonly causes no symptoms whatever while confined to that locality. Let it penetrate to the meninges, however, and a very serious illness results. Some bacteria while they have a preference for certain tissues may proliferate under conditions favorable to them in any part of the body. The streptococcus and tubercle bacilli may be cited as examples.

The ability of the pathogenic organism to multiply with a certain degree of rapidity is essential to the production of disease. In any case multiplication must exceed the natural rate of death, but the number must also develop faster than the increase in the specific defenses called into action by the presence of the organism, else clinical infection cannot result. Bacteria may develop more rapidly than the bodily defenses are able to kill them and yet because the body can form substances that neutralize the toxic products of bacterial growth faster than the organisms form them the so-called "carrier condition" results. The ability of an organism to gain entrance into and multiply in the body may be spoken of as its invasive power. It is different from, and may be entirely independent of, its virulence.

Virulence depends upon the organism's ability to develop products which are toxic to the tissues. Such toxins may be freely secreted and excreted by the organism or they may result only from disintegration of the cell. The former are designated as "exotoxins" or "true" toxins. They are extracellular and soluble and usually give rise to symptoms only after a period of incubation. The toxins of diphtheria and tetanus are the best known examples of exotoxins. The toxic products of most organisms can only be obtained by extraction or the disintegration of the cell, such toxins being designated in consequence as endotoxins. Much less is known about the "endotoxins" than the "exotoxins" and it is disputed that the former are specific products of the cell, Vaughan claiming that they are simply cleavage products of the protein of the cell protoplasm. His claim is that the differences in the clinical manifestations associated with different organisms are due to their differing predilections for certain tissues. He invites attention, for example, to the difficulty of differentiating meningitis caused by the pneumococcus from that caused by the meningococcus, without an examination of the spinal fluid. According to this theory, the specificity of the bacterial cell lies in a non-toxic fraction of the protein molecule and it is this fraction which gives specificity to the immunity resulting from an attack of a given disease or following the injection of a given bacterial vaccine. The virulence of an organism that does not form exotoxins then appears to lie in its ability to proliferate with great rapidity. Thus a streptococcus is said to be virulent because it is able to grow so rapidly as to overwhelm with its disintegration products the defenses it encounters in a number of different

individuals. With a single individual it might properly be questioned whether a severe infection was due to virulence in the parasite or lack of resistance in the host. The plague bacillus is virulent probably because comparatively few people have built up any specific defense against it.

The defenses of the body against infection are general and specific. The former are usually what we mean when we speak of one's "resistance." They operate with more or less efficiency against all infections. With the exception of the mechanical resistance offered by the uninjured healthy skin and mucous membrane and the mechanical, and for some organisms at least, the chemical effects of the secretions, the factors in resistance are probably for the most part specific. This specific resistance is what we commonly think of when we speak of "immunity" and is dependent upon the presence of certain ferments in the body fluids and upon the ability of certain cells to ingest and destroy invading organisms (phagocytosis). In part the latter is non-specific and to some extent it is dependent upon the non-specific as well as the specific opsonins in the blood. Opsonin is the name applied to substances in the blood which so act on a bacterium as to prepare it for phagocytosis.

While the general "resistance" of the body may constitute the principal defense against everyday infections and be an important factor in recovery from the specific infectious diseases, it is the specific substances in the body fluids which are mainly concerned in immunity. General "good health" has never proven a reliable defense against specific infections, although there is little doubt that it favors recovery once infection has been contracted. This is especially true in the common infectious diseases of childhood.

The specific immune substances fall into two general classes: First, those that are antitoxic and, second, those that are antibacterial. There is an important difference in the relationship between the exotoxins and their antitoxins as compared with the relationship of the endotoxins and the substances which neutralize them. Antitoxins combine with the corresponding toxins in (approximately) a multiple scale. Thus if one part of serum will neutralize one part of toxin, one hundred parts of antitoxin will neutralize approximately one hundred parts of toxin. No such scale obtains, however, in relation to the endotoxins. While a certain small amount of an immune serum may neutralize a certain small amount of a toxic filtrate, double the amount of serum will not neutralize double the amount of filtrate. The amount of serum must increase much more rapidly than the amount of filtrate and at a certain point neutralization becomes impossible no matter how much serum is added.

The immune substances of the body are conveniently grouped and spoken of as *antibodies* and except for the antitoxins and perhaps the precipitins they are for the most part antibacterial. Besides those mentioned, they in-

clude the agglutinins, the opsonins and the bacteriolysins, the first having the property of clumping bacteria, the second of preparing them for phagocytosis and the third of causing their dissolution. These are all for the most part specific for the homologous *antigen,* or *antibody producer,* although they exhibit their properties in a lessened degree for closely allied species. For example, the injection of killed typhoid organisms will produce not only agglutinins for the typhoid bacillus but also in smaller amounts for the paratyphoid bacilli A and B.

An antigen, as just mentioned, is an antibody producer. If a protein is injected into an animal body it will stimulate the body to produce antibodies to that protein if the dose employed is not so large as to cause death. The injection of diphtheria toxin stimulates the body to form antitoxin, the injection of typhoid bacilli stimulates the formation of typhoid antibodies. Living bacteria may be used as well as killed ones but as there would be difficulty in determining a dosage that would with certainty not cause a clinical infection, killed cultures are chosen. The immunity which people acquire "naturally" to many kinds of infection in the course of human existence is probably mainly due to their contact with antigens in doses so small as to produce only subclinical infections. Such contact also presumably increases the amount of non-specific and group antibodies and raises the immunity to infections allied to those with which they come in contact.

It cannot be too strongly emphasized that resistance and immunity, and, conversely, susceptibility are relative terms and that instances of absolute immunity under all circumstances are very few. Pasteur's experiment of placing in water a hen which is naturally immune to anthrax, thus rendering her susceptible to that disease, is a classical example of the relativity of immunity. Unusually virulent or large doses of infection or entrance by an exceptionally favorable route may overcome all but the most absolute of immunities. The dosage as well as the virulence of the infecting organisms is likewise an important factor in the severity of the subsequent clinical manifestations. The latter point is very apt to be overlooked and not improbably is a very important factor in determining the severity of an attack of measles and possibly of other infections.

Immunity has been classified as natural and acquired. Natural immunity is that which is inherent in the species or race. Species immunity is quite marked for certain infections, such as the immunity of birds and carnivorous animals to anthrax. The factors are not well understood but diet and body temperature appear to be important. Racial immunity while quite marked for some infections in certain varieties of lower animals is less marked in human beings. A relative immunity is to be noticed, however, in those races that have been exposed to a disease for many generations as compared with those into which the disease has recently been introduced.

Tuberculosis and measles are the classical examples usually cited to illustrate this immunity. So far as the latter is concerned it may be pointed out that immunity to the disease is still very rare even among the races that have been in contact with it for centuries and that the high mortalities reported among aborigines have been due almost entirely to the unintelligent care of the sick. It is worth remembering that in the Fiji Islands epidemic the whole population of a village was often taken sick at the same time so that each one had to care for himself; that as a result many died of actual starvation rather than the disease; that for the most part they treated themselves in the worst possible way and that the mortality in those few cases coming under the care of European physicians was but a small fraction of that among the untreated. In estimating the racial susceptibility to tuberculosis of aborigines it must likewise be remembered that their social customs and living conditions are such as to favor the spread of the disease among even a relatively immune people. There is need of great caution, therefore, in forming a conclusion as to racial immunity or susceptibility.

A certain amount of natural immunity is of course inherent in every one, else none could survive. In so far as it is specific, it is probably entirely passive, is dependent upon the antibodies elaborated by the mother and is usually quite effective against any ordinary dose of infection. A well-known example of this type of immunity is the immunity of babies to diphtheria and measles during the first few months of life. Non-specific natural immunity is probably only effective against small doses of the less virulent organisms and thus forms the base from which an acquired specific immunity may be built up with or without recognizable symptoms. This acquired natural immunity is active; that is, the cells of the individual's own body elaborate the immune substances—are active in their production. In contrast to passive immunity, which lasts only for a few weeks or a few months at most, active immunity may endure for years or even for a lifetime. Active immunity, as the result of an attack of the disease, has been recognized for centuries and as the result of an attack of a *modified or closely allied* disease, since the time of Jenner. Immunity may also be acquired *artificially,* and like the natural it may be either passive and evanescent or active and enduring. The former is exemplified in the administration of diphtheria antitoxin to the intimate contacts with a diphtheria case. This immunity is immediate. Artificial active immunity is exemplified in that resulting from the injection of diphtheria toxin-antitoxin mixture.

It is in his ability to confer immunity upon his clientele that the physician has one of his greatest opportunities to assist in reducing the incidence of, and mortality from, communicable disease. He should know the possibilities and the limitations of substances advocated as prophylactics, urge only those that are backed by adequately controlled experience and for which there is

likely to be need, and leave experiment to those who are in a position to carry it on with adequate controls. There is even less need for his heeding the brochures of the "biological house" than there is for prescribing drugs because of clever advertising. These prophylactics are, as a rule, susceptible to controlled experiment and unless there is general agreement among qualified investigators the product should be regarded as still in the experimental stage.

This is not to say that a physician is unwarranted in refusing to use an antitoxin or a vaccine under any circumstances because there is still doubt as to its exact value. No harm can come from advocating whooping-cough vaccine in the presence of the disease in the family or in the immediate neighborhood. He would not be justified, however, in recommending it as a routine as he would and should recommend vaccination against smallpox and inoculation with toxin-antitoxin against diphtheria. The two latter are quite certain to produce an immunity that will prove effective for several years against even heavy doses of infection. They materially modify the disease if the dose is unusually heavy and give a partial protection against ordinary doses even after so-called "complete" protection has gone. These prophylactics should be given in very early life for several reasons. Smallpox vaccination produces less reaction in infancy than later, and if performed by modern methods leaves a small scar which is scarcely visible in adult life. There is also not so great an opportunity for infecting the wound as there is after the runabout or even the crawling stage is reached and subsequent vaccinations do not produce the discomfort and possibly the temporary incapacity that primary vaccinations often do in the older child and adult. A child may be safely vaccinated on the leg before she has begun to crawl and creep—a practice that is not to be recommended at any later time. The physician must bear in mind that the type of smallpox prevalent to-day in Western Europe and the United States is almost never fatal, seldom permanently disfiguring and usually causes but little discomfort. We must be very certain, therefore, that our preventive therapy is correspondingly mild. The physician should remember too that the fanatical objections to vaccination have some foundation in practices common in former years and that while these practices may once have been unavoidable there is no excuse for them to-day. It is the physician to-day using a technic recognized as legitimate only ten or twelve years ago who is apt to bring discredit on the practice.

Inoculation against diphtheria with toxin-antitoxin should be done in infancy because it is during the first few years of life that diphtheria is most liable to kill. Despite the great benefit that may be expected from the early use of antitoxin in adequate doses, the fact remains that from one-sixth to one-fifth of the children who contract diphtheria before they are

five years old, die of it. It is immaterial to say that they could have been saved had this or that been done. Mistakes are being made every day by parents and physicians in judging the significance of the early symptoms. There would be few occasions for such mistakes if every infant were given toxin-antitoxin between the sixth and the ninth month after birth.

Aside from the duty of the physician to see that the family contacts of a case of smallpox or diphtheria are promptly immunized by vaccination in the one case and a prophylactic dose of antitoxin in the other, he has a further duty that is quite as important and almost as likely to save sickness or death. The importance of dosage of infection must be emphasized so that the family will keep a sick child isolated. If a child is known to have been exposed to measles or whooping-cough it is usually thought that all the damage that can be done has been done. Such a belief, if it is to be acted upon, should be supported by good evidence. As a matter of fact, there is good reason for believing that so far as measles is concerned dosage of infection is a very important factor in determining the severity of the primary disease. A child exposed once for but a brief period and at some distance will ordinarily have but a mild attack or escape clinical infection; one exposed day after day to massive doses at short distances will have a severe or perhaps a "malignant" infection. It seems reasonable to believe that a similar relationship exists in other diseases and that isolation of the sick should be insisted upon even though an effective exposure has probably already taken place. Such isolation is the duty of the attending physician quite independent of any law or of any further measures that may be taken by the health department to protect others outside the family.

This brings us to the duty of the physician to report to the health department diseases classed as notifiable. The question is often asked: "If I see to it that the patient is isolated, that no one leaves the premises who can carry the infection, why should I make a report? The health department can do no more than I have done except possibly to put up a placard." Placarding, which is often looked upon as one of the most important functions of the health department, is probably one of the least useful. It often is merely a gesture in response to the demand that, if the physician takes the trouble to report, the health officer must do something about it. The placard is an easy and not very intelligent way of "doing something." It is time-honored, respectable and impresses the laity. If it is all that a health department *can* do either for lack of funds or time or intelligence, it is perhaps better than nothing. There are better reasons for requiring reports, however, and they may not involve restricting or advertising the affected family at all.

Let us suppose that a child has developed whooping-cough or measles. He got it from some other case or carrier of that disease and he probably

has given it to some one else before he has been isolated. The source to which he was exposed may have caused other cases which in turn may be exposing still other susceptibles. The tracing of other possible cases is usually much more important than the strictest of "quarantines" for the known case. In smallpox such contacts should be vaccinated or held under observation; in diphtheria it may be advisable to give a prophylactic dose of antitoxin, or an atypical case may be recognized and properly treated before the toxin has been bound by the tissues. In measles the neighborhood may be canvassed and the parents of possibly exposed children warned of its danger to the very young so that they will be put to bed and placed under competent care from the onset of the fever, or convalescent serum may be given to poor risks that have been definitely exposed. Something of the same kind may be found feasible in whooping-cough and scarlet fever; diseases in which the case fatality rates are still high in the first few years of life.

The pediatrist and general practitioner share with the health officer the opportunity to advance our knowledge of the occurrence of the infectious diseases of children through observing, recording, collecting and tabulating certain rather simple facts. The observing and recording are the functions of the practitioner; the collecting and tabulating that of the health officer. It also devolves upon the latter to analyze and interpret the tabulated figures, although every one is free to draw his own conclusions once the facts have been assembled in an intelligible set of tables.

Of course any practitioner in the course of time can collect and tabulate his own recorded observations, but these are apt to be of less value than those received from varied sources because of the likelihood of their being more or less one-sided. Infectious diseases among the rich differ quite decidedly from the same diseases among the poor. They are more likely to be fatal among the latter, partly due to the earlier age at which they are attacked, partly to the less favorable environment and to the less prompt and less intelligent care which they receive when taken sick. Few if any physicians have practices which represent a true cross section of the community. He is almost sure to have a preponderance of cases from one class or another as compared with the relative number of persons of that class in the community. His experience will be colored accordingly.

It is important, therefore, that the physician report even for the report's sake and that he be not too urgent in his demands that the health department "do something about it."

CHAPTER II

SCARLET FEVER

Definition.—Scarlet fever is an acute communicable disease occurring most frequently in the first decade of life. It is characterized by sudden onset, vomiting, sore-throat, fever. These symptoms are shortly followed by a generalized scarlet cutaneous eruption, after the subsidence of which desquamation occurs.

Synonyms.—Scarlatina, Scharlach, la scarlatine.

Historical.—There can be no question that the disease has existed from time immemorial but it was not clearly differentiated until 1676, when Sydenham applied the term scarlet fever to distinguish it from other fevers characterized by a rash. Up to that time measles, diphtheria and scarlet fever had been grouped as one disease. A remarkably accurate description of this latter disease was written in 1736 by a Boston physician named Douglass. The title of his pamphlet was "The Practical History of a New Epidemical Eruption Miliary Fever with an Angina Ulcusculosa Which Prevailed in Boston, New England, in the Years 1735 and 1736." Bartlett in 1810 claimed that this treatise was the first real contribution of America to the medical literature of the world. Weaver found that Douglass was born in Scotland in 1695 and settled in Boston in 1720, where he died in 1752. He recognized the epidemic character of the disease and traced the course of an epidemic in Boston and through New England. Boston at that time had a population of about twelve thousand and of these about four thousand contracted the disease. The mortality rate was not very high as only one in thirty-five died, which compares very favorably with the mortality rate of the present day. He recognized the principal symptoms as well as the complications and described mild as well as severe cases. Benjamin Rush studied an epidemic in Philadelphia in 1783 and since that time a vast number of articles have appeared in medical literature describing epidemics, theories regarding the cause of the disease, its pathology, etc. There was much confusion between scarlet fever and diphtheria which was not cleared until the recognition of the Klebs-Löffler bacillus and a ready method of its bacteriological diagnosis of diphtheria had been introduced and made available to the general practitioners of medicine.

Etiology.—Children are much more susceptible to scarlet fever than adults but there is a natural immunity to this disease in a large number of

persons. Possibly less than half who are exposed will contract scarlet fever. That members of certain families are more susceptible than others is proved by the fact that during an epidemic in which most of the cases are extremely mild all the children in these susceptible families may develop severe cases.

Age.—Infants under one year of age are seldom infected but this may be due to the fact that they are not exposed to such an extent as older children. When young infants contract scarlet fever the mortality is very high. Statistics show that about one-half of all cases occur in children from three to seven years of age. After the tenth year the susceptibility declines and adults rarely contract the disease.

Occurrence.—Epidemics are more frequent in the winter and early spring. The lowest incidence is in midsummer. Cases occurring during the winter months are apt to be more severe. This seasonal variation is undoubtedly due to closer indoor association and greater opportunity for exposure. Older children who may be exposed in school carry the infection back to their homes and infect younger brothers and sisters. In winter also there is liable to be more crowding and less ventilation in homes, schools, theaters and churches. At this season colds and catarrhal affections of the throat and nose are frequent and this undoubtedly increases susceptibility to infection.

Race.—There seems to be a racial immunity among negroes, for the official United States Census Statistics show that the mortality is much less among the black than the white population. Dublin, from the Metropolitan Life Insurance Company statistics, found that the death rate among the colored race was about one-fourth that of the white.

Bacteriology.—There is no question but that scarlet fever is caused by a specific organism or virus. By analogy to other communicable diseases whose specific organism is known, scarlet fever must be transmitted by contact with carriers or individuals ill with the disease. Up to this date there has been no definite and positive identification of this organism. There has been a tremendous amount of investigation and research work, the history and description of which would fill volumes. The rôle of hemolytic streptococci has been studied for many years and almost all observers have been impressed by the constant presence of this type of organism in the throat and often in the blood stream. Maer, in 1899, isolated over thirty different strains of streptococci from blood taken from fatal cases of scarlet fever. Many recent observers have obtained toxins from streptococci grown from cultures taken from the throats of scarlet fever patients. These toxins have been neutralized by convalescent serum. The streptococci belong to a distinct biologic group known as "β-hemolytic." Dick and Dick claim to have been able to reproduce the disease in humans by inoculations of this

streptococcus. The claim is made that the scarlet fever streptococcus differs from those obtained from other diseases. Hektoen, who has made a careful study of the bacteriology, is doubtful whether a definite and positive result has been found. Nevertheless great advance has been made in the past five years and it is not unwarranted to hope that in a short time we shall have the same control over scarlet fever as we now have over diphtheria.

Epidemiology.—With our recognition of the presence of the infective agent in the secretions and excretions of cases of scarlet fever we can determine the ways and manner by which it may spread. Not alone from our knowledge of the bacteriology but from clinical experiences there can be no question that the infecting agent of scarlet fever is present in the secretions from the respiratory tract, discharges from the middle ear, mastoid and from suppurating glands. The old belief that the disease was spread from the desquamated scales of the skin has been discarded. Healthy carriers play an important part in the spread of scarlet fever. Toys, clothing, books, bedding, etc., when contaminated by discharges of infected persons may be occasionally responsible for the dissemination of this disease. The domestic fly and perhaps other insects may carry the disease to susceptible persons. The only food which seems to convey scarlet fever is milk. A large number of widespread epidemics have been found to have been caused in this manner. Such outbreaks have been studied with great care and the rôle of the infected milk has been definitely and thoroughly proved. A scarlet fever patient, convalescent or carrier handling milk may readily infect it either during the milking or the bottling process. There is absolutely no reason to believe that air can carry dry germs in a virulent form, for drying rapidly kills bacteria. Close contact with a patient seems to be necessary in order to become infected. It is extremely doubtful if the infecting agent can be transmitted by a third unaffected person. The tenacity of the virulence is variable and it seems capable of living a long time, for instances have been reported where it was capable of infecting healthy susceptible persons after 133 days. It is difficult to destroy and resists most attempts of popular methods of disinfection. The period of highest infectiveness is just before the onset of acute symptoms. It is capable of being spread for months if there is a persistent discharge from the ears or nose. The mode of entrance of the germ is not definitely known, but a large amount of evidence points to the upper respiratory tract, especially the tonsils. From here it spreads through the entire system. In surgical scarlet fever the infecting agent enters through the open wound.

Pathology.—There are no gross pathological lesions found in scarlet fever and very little is found postmortem which is characteristic of the disease. The skin shows an acute dermatitis with areas of erythema and

minute hemorrhages. This dermatitis is followed by death of the affected skin, which results in dequamation. The mucous membrane of the nose, mouth and throat shows a catarrhal inflammation which may be so severe as to become membranous or even gangrenous with destruction of the under-lying tissues. The inflammation may extend to the middle ear, nasal sinuses, mastoid cells and even the meninges. The lymph-nodes in the region of the neck are frequently enlarged and may go on to suppuration. The axillary glands and those in the groin are also enlarged. This hyperplasia of the lymph glands is more marked and frequent in children. The visceral lesions are degenerations due to the action of the toxin, those in the kidney being of great importance. In the early stage there is simple degeneration and it may later develop into an interstitial nephritis. A true glomerulo-nephritis may develop in the third or fourth week. The cells of the con-voluted tubules undergo destruction and desquamation. There may be complete recovery from these lesions or it may develop into a chronic nephritis. It is remarkable how some patients whose kidneys were thus permanently injured have lived many years without any discomfort or symptoms of chronic nephritis.

SYMPTOMS

The symptoms of a typical case of scarlet fever are: Sudden onset, sore-throat and vomiting, rapid rise of temperature, early appearance of an erythematous rash, enlargement of the cervical lymph-nodes, and a peculiar appearance of the tongue. But scarlet fever presents more variations in its manifestations than any other eruptive fever.

Incubation Period.—The incubation period is short, the majority of cases developing in from two to five days after exposure. Cases showing symptoms twenty-four hours after exposure are occasionally seen. On the other hand, symptoms so rarely develop in the second week after exposure that eight days is considered the limit of liability of attack. In cases reported as occurring two weeks after exposure some more recent avenue of exposure has doubtless been overlooked.

The Onset.—The prodromal stage is short and is likely to be overlooked, especially in children. An unexplained attack of severe vomiting usually marks the beginning of the disease. This symptom, which seldom persists beyond the first day except in toxic cases, is almost constant in young chil-dren but may be absent in older children and adults. Chilliness or rigor may be present at the onset and in young children a convulsion is not uncommon. Diarrhea occurs at times.

Sore-throat is a constant and early symptom without which a diagnosis should not be made. This is accompanied by a rapid rise in temperature

and the usual subjective accompaniments of fever; prostration and muscle pains are noted.

The Temperature.—The temperature rises rapidly from the onset and may, within thirty-six hours, attain its maximum of 100° to 104° or 105° F., depending upon the severity of the attack. The highest point is commonly at the height of the eruption and it continues high with slight or moderate remissions until the eruption begins to fade, then falls in a stairlike manner, reaching the normal level in a week to ten days. A variation in this characteristic curve is usually an indication of complications. Very mild cases are almost apyretic. In hospital and private practice the initial rise is not often observed as usually the temperature is almost at its peak when the patient is first seen.

Pulse and Respiration.—The pulse is accelerated out of proportion to the elevation of the temperature. A rate of 130 to 140 is common and one mounting to 160 in a young child does not necessarily mean a bad prognosis. Respiration is little affected.

The Eruption.—The eruption usually appears within twenty-four hours of the initial vomiting, but it may appear as early as twelve hours or it may be delayed in rare cases to the fourth or fifth day. It is usually well developed by the second day, continues from four to six days and then subsides gradually. It begins on the sides and the front of the neck and spreads rapidly downward. When fully developed it is most marked on the neck, back and chest, particularly in the axillary region, the abdomen, groin, the inner surface of the thighs and the buttocks. The typical eruption does not usually invade the face, but when it is involved it is limited to the bridge of the nose, the temples and the forehead. The cheeks are deeply flushed and the area around the mouth becomes dead white which gives the striking and characteristic picture of *circumoral pallor*. Viewed from a distance and in bright daylight the patient presents the picture of flushed cheeks, marked paleness about the mouth and the body painted a bright red. Close examination shows the rash to consist of minute points of bright red upon a hyperemic skin. In places they become confluent, forming bright red areas, while if the punctæ are widely separated the skin may be normal in color between them. The skin in brunettes becomes a dusky red and in negroes it is rather bluish. There may be papules of sufficient elevation to impart to the fingers a sensation of roughness resembling goose-flesh. Tiny vesicles may be observed especially in front of the axilla and on the abdomen. Below the knees and elbows and involving the hands a blotchy appearance resembling measles is sometimes seen. Petechial areas, even in mild cases, are sometimes present, often upon the dorsum of the feet or any area subject to pressure.

Special diagnostic signs for the eruption have been described, many of

them of little value. The efflorescence fades upon pressure, due to its hyperemic character, but immediately reappears except in cases where the circulation is feeble, when the outline of the hand remains for some time. The rose-colored linear exanthemata, two to four in number on the anterior surface of the elbow, designated as Pastia's sign, are nearly always present and are of diagnostic importance.

The great variation in the time of the appearance of the eruption and its distribution renders diagnosis difficult. That scarlet fever may be present without any noticeable rash appears evident from the number of cases of sore-throat which are coincident with an epidemic of scarlet fever. Occasionally the rash appears only on the lower part of the body. The eruption may spread rapidly downward from the chin and involve the lower extremities by the end of the first twenty-four hours or the course may be much slower and that on the upper part may begin to fade before it has reached its height on the lower part of the body. The eruption usually lasts from four to five days and a yellow staining often remains after the eruption fades. Slight eruptions which last less than twenty-four hours are probably not scarlet fever.

The Tongue.—The progressive changes that take place in the appearance of the tongue are of great diagnostic importance. Nicoll describes these as follows: "At the end of the first day of the disease the tongue is covered with a grayish white coating, and on the second day the tip and edges begin to shed their coating and present a red boundary line to the white center. The coating is now pierced by numerous red swollen papillæ. During the third day the process of desquamation continues; on the fifth and sixth day it is practically complete, except usually for a slight remaining coating in the back median line, and there is presented the typical strawberry or cat's tongue, brilliantly red, dotted with swollen and protruding papillæ. These gradually subside, leaving a smooth, glazed tongue with little or no coating, comparable in appearance to raw beef, after which the normal coating returns. The appearance of the strawberry tongue may be delayed, and in many cases the evolutionary process is not so definitely or clearly marked as has been described."

The Throat.—The primary lesion of scarlet fever is in the throat and without some inflammatory changes there the diagnosis cannot be made. There is, however, no typical scarlet fever throat. All grades of inflammation from moderate pharyngitis to a membranous or even necrotic process are possible. Early in the disease inspection of the throat reveals redness and swelling of the palate, uvula and tonsils. Usually the uvula is red and edematous and upon the reddened palate punctæ of darker red, characteristic in appearance, are discernible before the rash has appeared upon the skin. The tonsils are swollen and exhibit spots of creamy or grayish

exudate due to the streptococcic involvement. There may be few subjective symptoms, or on the other hand the changes may be so marked as to constitute the chief element of suffering. Pain on swallowing, tenderness behind the angle of the jaw and enlargement of the cervical lymph-nodes are usual.

The Desquamation.—Following the disappearance of the eruption, usually at the end of the first week, desquamation begins. As already noted, the process begins on the sides of the tongue. On the skin the cuticle is first shed from the sides of the neck and the ear lobes in the form of powdery scales. The miliary vesicles become centers of areas of desquamation which spread centrifugally to form irregularly rounded patches with rounded margins. The scales may be powdery or of considerable size. The process proceeds downward over the chest and back. Upon the hands the first break is seen at the free margins of the nails. The skin of the fingers and palms is shed in large thick masses and may even be cast off as a complete glove. The feet are involved later. The entire process extends over a period of three weeks or longer, and occasionally a second desquamation follows the first.

Other Symptoms.—Cases of moderate severity at times show marked restlessness and even a mild delirium at night. This is not of particularly grave significance. The *urine,* which during the febrile period is scanty and dark-colored, may show a trace of albumin and a few blood-cells and casts even in the absence of actual nephritis. The *blood* shows a marked polymorphonuclear leukocytosis, 15,000 to 30,000, which attains its maximum at the height of the rash. The *lymph-nodes* of the axillæ and groin as well as those of the cervical region are almost always enlarged.

TYPES OF THE DISEASE

The diverse manifestations of scarlet fever make a description of the usual types desirable. Cases range in severity from those so mild as to leave diagnosis in doubt until desquamation begins to those so overwhelming in toxemia that death terminates the case before the characteristic symptoms of the disease have time to develop.

Ordinary Type.—The usual case of moderate severity is ushered in by a rapid rise in temperature, vomiting without apparent cause, soreness and congestion of the throat. The temperature climbs to 104° to 105° F. in the first twenty-four hours, while the pulse rate runs from 120 to 160. The throat becomes red and edematous and a punctate eruption spreads over the soft and hard palate. The tongue is heavily coated, except at the edges which are bright red and show enlarged papillæ. By the second day the eruption is well developed on the neck and chest, the cheeks are flushed and the area around the mouth is white. As the disease progresses the

eruption spreads downward. The lymph-nodes of the axillæ and groin are palpable by the second or third day. The temperature falls a little daily until the normal level is reached in a week or ten days. The tongue desquamates, the rash fades and the cuticle is shed from above downward. The patient is left weak and anemic, and still subject to late complications, but if these do not intervene he rapidly regains health.

Mild Type.—Cases which are without doubt scarlet fever but are so mild as to be likely to escape detection were it not for the history of exposure are frequently observed in connection with other cases in a family or institution. In such cases the rash is so poorly developed as to be difficult to recognize, but it persists for at least twenty-four hours. The throat may show only a mild pharyngitis, the temperature be but slightly elevated, although it may reach 101° or 102° F. for a short time, and the pulse be more rapid than should be expected from the temperature. In due time a desquamation confirms the picture of scarlet fever.

Toxic Cases.—The classification of toxic, septic and malignant scarlet fever is largely one of the degree of an intense septicemia. A severe toxemia may be inferred to be an individual response to the infection rather than due to an especially virulent organism since toxic cases occur during the prevalence of a mild epidemic. In the so-called *malignant* cases the patient is overwhelmed by the toxemia before the typical symptoms of scarlet fever have time to develop. There are chills, intense headaches, frequent vomiting and a severe diarrhea. The fever is high, the pulse rapid and thready, but the rash is not typical as the entire skin appears congested and bluish and petechiæ are observed in various parts of the body. Convulsions and delirium in children are the rule. Death terminates the case in from twenty-four to thirty-six hours after the temperature has reached an extremely high level.

Septic Scarlet Fever.—This type owes its characteristics to the associated organisms, usually hemolytic streptococci. These organisms, which are commonly present in the throats of scarlet fever patients, develop marked virulence in some cases. A conspicuous swelling begins in the tonsils which show patches of grayish white or yellow exudate. Culture of these patches reveals various types of streptococci. The surrounding tissues of the pharynx are swollen and red and an intense inflammation involves all the glands and tissues of the neck which become tense and swollen. As the disease progresses the pharynx and nasopharynx become ulcerated and a mucopurulent, often bloody secretion is discharged from the nose and throat. The pain in the throat is so intense as to interfere both with breathing and swallowing. From the throat, extension of the infection to the middle ear and mastoid takes place early in the disease.

The eruption in this type does not differ from the usual case of scarlet

fever, but secondary rashes sometimes appear. The temperature is high and remains so while the throat involvement lasts. There is a marked leukocytosis and blood cultures may show streptococci. This septic type is more liable to affect children than adults. The picture is that of a child critically ill, and restless or delirious. Death may be due directly to general septicemia, failure of the circulation or a secondary bronchopneumonia.

Surgical Scarlet Fever.—Cases of apparent scarlet fever which follow closely upon some mechanical injury such as burns, lacerations, vaccinations and delivery occur in hospitals and private practice. Some of these cases are pure coincidences, others may have rashes due to toxic substances absorbed from wounds, to chemical agents used as antiseptics or they may be produced by bacteria which are not the organisms of scarlet fever. Excluding all such doubtful cases there still remains a residue which develops the typical symptoms of scarlet fever, sore-throat, leukocytosis, fever and subsequent desquamation as well as the typical rash. The mechanism of the infection is conjectural, but it seems probable that the organisms gain a foothold through the weakened resistance of the injured skin or mucous membrane. These cases seem to be especially likely to follow operations on the nose or throat or for cleft-palate.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Diagnosis of the typical case of scarlet fever presents few difficulties. The symptom-complex consists of sudden onset with sore-throat and vomiting, rapid rise of temperature and a disproportionate acceleration of the pulse, the early appearance of an erythematous rash and the peculiar appearance of the tongue. However, many atypical cases of scarlet fever occur and other conditions resemble scarlet fever so closely that the experienced physician at times encounters difficulties and is forced to a careful weighing of evidence of history, symptoms, appearance and clinical course.

In *measles* the catarrhal symptoms predominate in the eyes, nose and bronchi, while the throat is little affected. The strawberry tongue is absent, but the eruption of Koplik's spots on the buccal mucous membrane can be detected before the rash appears. The later appearance of the rash (usually the fourth day) and its papular and blotchy character aids in the differentiation. In many places it is surrounded by areas of healthy skin and the area around the mouth is not spared. There is no leukocytosis.

In *rubella* the incubation period is longer, the invasion is mild without vomiting, the throat is only slightly sore and the catarrhal symptoms are usually slight. The postcervical glands are enlarged. The rash appears first on the face, is commonly fleeting and consists of discrete rose-red spots. The desquamation is negligible. There is no leukocytosis.

Diphtheria may be suspected on account of the false membrane which forms in severe cases of scarlet fever or conversely diphtheria may suggest scarlet fever when it is accompanied by an erythema. Furthermore the two diseases are sometimes coexistent. The false membrane of diphtheria is thick, grayish white and firmly adherent, throat cultures show the presence of diphtheria bacilli and the rash is transient. The strawberry tongue does not occur in diphtheria.

Acute follicular tonsillitis begins abruptly with a high temperature but the tongue is not red and papillated and if an erythema occurs it is limited, transient without punctation and is not followed by desquamation.

Septicemia may be accompanied by an erythematous rash but there are also evidences of local suppuration and the fauces and tonsils are not swollen.

Erythema scarlatiniform is a condition of unknown origin but probably related to a disturbance of the gastro-intestinal tract. The eruption is irregularly distributed, is erythematous, but not scarlatiniform in appearance throughout. There may be an initial chill and slight fever but on the whole the constitutional symptoms are mild. There is usually a history of a previous attack. There is early and profuse desquamation.

Drug eruptions such as those caused by quinin, copaiba, the various coal tar products and antitoxic sera are not usually generalized and are not associated with sore-throat and strawberry tongue. Erythemas associated with a digestive disturbance in young children are often very suggestive of scarlet fever, except for the transient nature of the rash.

Skin Blanching Test.—Shultz and Charlton in 1918 described an intradermal test which has proved to have undoubted value in the diagnosis of scarlet fever. They found that if the serum of a person convalescent from scarlet fever was injected into the skin of a patient with acute scarlet fever it would produce a small area of blanching or local cure at the site of injection. This phenomenon did not occur when the suspected rash was due to causes other than scarlet fever.

There is no question but that many cases of streptococcus infection associated with sore-throat have been diagnosed and treated as scarlet fever by experienced physicians. The blanching test affords a means of arriving at a definite diagnosis. While it is not an absolutely dependable test, yet it is of great diagnostic value in many doubtful cases.

The technic of the test is simple and the serum can be obtained from many state health laboratories as well as from commercial houses. From ½ to 1 c.c. of serum is injected intracutaneously where the rash is well marked. The injection is made in the same manner as the Schick test but is given in the skin of the chest, abdominal wall or thigh. The white area appears in a few hours and may persist until the general rash fades.

COMPLICATIONS

Were it not for the possible complications, a simple case of scarlet fever would not be feared and dreaded. Complications follow or accompany fully 40 per cent of all cases of scarlet fever.

Adenitis.—There is some enlargement of the cervical lymph-nodes in every case of scarlet fever. In severe cases the swelling is more pronounced and may terminate in suppuration, associated with a secondary rise in temperature. The glands enlarge while the throat is still inflamed and may not develop until a week or ten days after the onset of the disease. If an abscess forms it may break spontaneously if not incised or may perforate into the pharynx. Suppuration occurs in about 5 per cent of cases. The infection may pass into the tissues surrounding the glands and cause great swelling and induration of the neck and cervical tissues. The ears are surrounded by the mass of swelling and the eyes are swollen and edematous. There is general sepsis and the tissue shows a diffuse necrosis with no formation of pus.

Otitis media and Mastoid.—The middle ear is infected in a large percentage of cases, and infection is especially frequent in young children. It is usually present in cases in which there is a marked involvement of the throat. The frequency of this infection varies in different epidemics. It most often appears about the end of the first week but it may not be seen until late in convalescence. The attending physician should make a daily inspection of the ear-drums and on the first appearance of a bulging membrane he should make an early incision. The discharge is at first muco-purulent, later purulent, and is liable to continue for weeks or even months. As a rule both ears are affected. There is usually no permanent impairment of hearing but when it occurs in young children deaf-mutism may result. In these cases the ossicles and tympanic membrane are destroyed. Of cases of deaf-mutism about one in ten results from otitis following scarlet fever. The mastoid is involved in a small percentage of cases secondary to otitis media and should be suspected if there is pain and tenderness back of the ear.

Kidneys.—A transient albuminuria is present in a large number of cases especially when the fever is high. It is the result of the temperature and does not necessarily mean that the kidneys are involved. This albuminuria occurs during the height of the acute symptoms and casts and blood may be found in the urine which should be examined daily during the acute stage of the disease and at least once a week for the following month. Nephritis is one of the most frequent complications of scarlet fever in young children. It appears most frequently from the second to fourth week, is usually an acute diffuse condition with more or less involvement of the glomeruli of the kidneys, and is called postscarlatinal nephritis. The onset

is usually abrupt with a rise in temperature, sometimes convulsions, vomiting, and suppression of urine, with or without dropsy. It may, on the other hand, be gradual with increasing anasarca. The urine is diminished in quantity, dark in color and contains blood, albumin and casts of all varieties. Later the color becomes lighter and there is less blood and the amount of albumin and casts is diminished. Edema is present in most of the cases and the patient becomes anemic. The systolic blood-pressure is increased. Headache is a frequent symptom. A severe attack of postscarlatinal nephritis may follow a mild attack of scarlet fever. Some authorities believe the onset of nephritis is dependent in some degree on the diet and that children who are kept on a mild diet are less apt to have involvement of the kidneys. Catching cold and exposure to drafts during convalescence are probable factors in producing the condition.

The course of the nephritis depends on the age, constitution and the treatment the child receives. The symptoms may only last a few days and the case terminate in a quick and complete recovery. Permanent recovery is the rule even when the nephritis lasts several weeks for it is rare to have the kidneys permanently damaged as a result of this complication. The most dangerous symptom is uremia which may develop rapidly with or without suppression of urine. Death nearly always results from the convulsions caused by uremia. A small percentage of the cases becomes chronic. Children who have had postscarlatinal nephritis are more susceptible in later life to affections of the kidneys.

Arthritis.—Pains in the joints are not at all infrequent and vary in different epidemics. They may occur during the eruptive stage or in the second or third week. Arthritis is infrequent in children under four years of age. In this it resembles acute articular rheumatism but the endocardium is very rarely affected. The joints of the hand, wrist, elbow or knee are most frequently involved, and usually several joints are attacked simultaneously. There is a rise in temperature preceding or accompanying the joint pains. The joints are swollen and tender on motion and on touch. The condition may last only a few days or may be prolonged for several days. Blood cultures in a series of these cases were sterile. The chronic cases may result in permanent disuse of one or more joints from thickening and ankylosis. Acute enlargement of the joints may be of septic origin and go on to suppuration. The large joints are generally the ones involved and the lesions are apt to be multiple.

Heart.—Heart murmurs are frequently heard during the acute stage of scarlet fever. These are purely functional and disappear entirely during convalescence. In the septic cases a true endo- or peri-carditis is apt to develop with a fatal termination. Permanent injury to the endocardium even in cases associated with arthritis is rare. Pericarditis is occasionally

met with. The murmurs heard in the acute stage are the result of myocarditis but they disappear after a few days of rest in bed.

Lungs.—The lungs are rarely involved in scarlet fever. Bronchopneumonia is only found in septic cases or long-continued illness which is the result of other complications. In this respect scarlet fever differs from measles. Pleurisy with serous effusion may occur in young children but in older children the effusion is more frequently purulent in character.

Digestive System.—Vomiting is a characteristic symptom of the onset of scarlet fever and it may persist for several days. Complications on the part of the alimentary tract are not common or characteristic of the disease. Diarrhea is more frequent than constipation. The tongue at first is coated but in a few days becomes shiny red with enlarged papillæ, the so-called strawberry tongue. There may be an ulcerative stomatitis with bleeding gums and loosening of the teeth. In rare conditions, more especially in institutions and asylums, this stomatitis may develop into gangrene involving the mucous membrane of the cheek. This is more frequent after measles.

Blood.—A secondary anemia is present in all of the severe cases and lasts well into convalescence. There is reduction of 20 to 30 per cent in the hemoglobin and about a million in the red cells. A leukocytosis is present which is most marked in the first week of the disease. This may reach to twenty-five or thirty thousand. During this stage the eosinophils are decreased while the polymorphonuclear neutrophils are increased. After the first week the percentage of eosinophils increases. In malignant cases there may be no leukocytosis and no increase in the eosinophils. The blood findings are of value in diagnosis. Fatal hemorrhages from eroded blood-vessels in the neck, ear, nose and throat have been reported.

Scarlet fever may be complicated by other infectious diseases, for any one or more of the communicable diseases may appear in the course of the disease. The most frequent is diphtheria. It may be of the nasal type or involve the throat or larynx. It is a dangerous complication and may escape recognition as the discovery of its presence is only possible by culture and the finding of the Klebs-Löffler bacillus. Every case of scarlet fever in which a membrane is present should be cultured. The rapidly extending use of toxin-antitoxin will reduce the danger of this complication. Prompt recognition and use of antitoxin is necessary to prevent death by diphtheria and general septicemia.

Measles complicating scarlet fever is a serious condition especially in infectious disease hospitals and children's institutions. When it develops in a child already weakened from scarlet fever the danger from bronchopneumonia is greatly increased.

Cases complicated with German measles, chickenpox, smallpox, erysipelas

and typhoid fever have been reported. The symptoms are a combination of both diseases, although one may develop while the other is subsiding.

Recurrences.—Authentic instances of relapses shortly after the first attack have been reported. This refers to cases appearing within four or five weeks. These relapses most frequently occur during desquamation and are accompanied by vomiting, fever and a new eruption. They are comparable to relapses occurring in typhoid fever. Second attacks of scarlet fever rarely if ever occur, as one attack generally affords immunity for life.

PROGNOSIS

The chief dangers in connection with scarlet fever lie in the complications. The mortality in simple cases beyond the age of infancy is very low although it varies in different epidemics. Simple cases may later develop serious and even fatal complications, so it is extremely difficult to foretell the outcome. No one can predict that complications will not develop until desquamation has ceased and at least four weeks have passed. In epidemics of the mild type the mortality may be as low as 4 per cent, while in others of a more malignant type it may reach as high as 40 per cent. The mortality in infants is higher than in older children. It is also liable to be higher in hospitals and institutions for children. It is higher among the poorer classes where there is more crowding than with the well-to-do.

Death is almost certain in the septic or malignant cases. Bronchopneumonia in young children is liable to prove fatal. The coexistence of diphtheria renders recovery less likely.

The following tables are of interest in considering the prognosis of scarlet fever. Both the mortality and morbidity figures show a diminution in the summer months and a marked increase during the winter months when children come in close contact in the schools.

TABLE I.—MORTALITY FROM SCARLET FEVER IN NEW YORK STATE PER 100,000 POPULATION FROM 1915 TO 1925, ACCORDING TO MONTHS

Year	Jan.	Feb.	Mar.	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1915	5.5	6.6	6.1	8.4	10.2	6.1	2.6	1.1	.4	1.3	.9	1.4
1916	2.7	1.6	3.1	3.4	2.2	1.8	1.3	.5	.2	1.1	1.6	1.8
1917	1.9	2.2	4.1	5.1	4.3	2.8	2.3	.8	.8	1.4	1.9	3.1
1918	5.8	4.2	4.3	4.6	3.9	3.1	1.8	.8	.8	2.2	1.3	2.1
1919	4.3	3.2	5.5	3.2	3.1	2.2	1.9	.6	1.5	1.4	1.8	2.5
1920	4.3	6.3	3.5	4.0	4.6	4.1	2.7	2.1	2.7	3.3	4.4	9.7
1921	12.9	10.8	11.2	10.7	8.4	5.4	2.0	1.6	1.5	2.0	4.8	4.4
1922	6.1	7.5	8.2	7.3	4.8	4.0	1.9	1.0	1.4	2.5	2.0	2.8
1923	3.0	4.4	3.0	5.3	3.6	2.3	1.5	.9	.4	1.4	1.6	2.8
1924	3.9	4.0	4.1	4.8	3.1	1.9	.7	.6	.6	.6	1.7	1.8
1925	2.5	3.3	3.7	2.4	2.4	1.3	.4	.5	.3	.9	.7	1.3

TABLE II.—MORBIDITY FROM SCARLET FEVER IN NEW YORK STATE PER 100,000 POPULATION FROM 1915 TO 1925, ACCORDING TO MONTHS

Year	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1915.....	212.0	243.7	267.4	298.5	245.6	176.5	80.3	41.0	39.3	74.7	108.3	133.6
1916.....	154.1	164.9	184.8	181.0	161.7	110.0	62.4	23.1	28.5	53.5	89.2	118.5
1917.....	168.6	219.8	260.1	291.7	202.9	129.7	66.9	32.1	52.4	94.2	143.6	151.2
1918.....	154.0	150.2	161.7	160.5	121.9	77.0	50.8	34.5	49.1	68.1	65.4	95.1
1919.....	124.8	162.2	177.4	145.7	138.3	86.1	50.7	32.6	64.3	103.3	138.0	182.1
1920.....	184.0	166.1	175.5	166.1	165.2	120.6	61.9	43.3	56.7	110.1	194.0	299.4
1921.....	434.7	468.5	404.8	318.1	248.8	194.9	65.9	51.8	81.2	140.9	226.6	286.5
1922.....	313.7	346.9	339.9	274.5	268.5	136.7	67.7	49.7	72.8	123.4	196.5	223.7
1923.....	268.3	298.9	310.7	273.3	249.5	172.2	74.2	45.8	58.9	97.8	182.7	240.4
1924.....	295.9	317.0	335.6	325.0	251.3	174.3	73.5	37.9	48.9	91.0	162.4	242.3
1925.....	267.3	334.8	332.3	315.7	252.6	133.0	82.3	28.7	37.8	76.7	116.1	158.3

TABLE III.—MORTALITY RATES IN SCARLET FEVER PER 100,000 POPULATION IN THE UNITED STATES REGISTRATION AREA AND IN RURAL AND URBAN SECTIONS OF NEW YORK STATE

Year	United States Registration Area	New York State	New York City	New York State, Exclusive of New York City
1915	3.6	4.2	5.6	2.6
1916	3.3	1.8	1.8	1.7
1917	4.2	2.6	2.2	2.9
1918	3.0	2.9	3.2	2.5
1919	2.8	2.6	2.4	2.8
1920	4.6	4.3	3.9	4.8
1921	5.3	6.3	6.8	5.7
1922	3.5	4.1	3.8	4.5
1923	3.5	2.5	1.9	3.3
1924	..	2.3	1.4	3.3
1925	..	1.6	1.3	2.0

TABLE IV.—MORTALITY RATE IN SCARLET FEVER PER 100,000 POPULATION FROM 1915 TO 1924 ACCORDING TO AGE

Age, Years	Number		Rate		Per Cent of All Cases	
	1915	1924	1915	1924	1915	1924
Under 1.............	18	11	7.4	4.7	.1	.1
1	52	29	27.9	13.6	1.0	.9
2	70	39	35.3	17.8	3.4	2.6
3	66	21	33.9	9.5	5.1	2.3
4	27	25	14.4	11.7	3.0	3.2
5-9	105	50	11.7	4.8	3.8	1.9
10-14	33	20	3.9	2.1	1.9	1.1
15 and over	44	59	.6	.7	.04	.1
TOTAL ALL AGES	415	254	4.2	2.3	.3	.2

TREATMENT

Prevention.—Every effort should be made to prevent the spread of scarlet fever and each case must be isolated and quarantined until all danger of infection is passed. Young children are more susceptible and greater protection should be afforded them. As the disease is transmissible before the appearance of the rash every suspected case should be at once separated from other members of the family. A mild case requires as rigid isolation as a severe one. Children who have come in contact with a case of scarlet fever should be carefully observed, viewed as suspects, and kept from mingling with other children until the period of incubation has passed. If proper isolation cannot be secured at home the child should be removed to a contagious hospital. In cities where such hospitals exist this is the best and safest procedure even though a suitable quarantine can be secured in the home. When the child is treated at home a room with connecting bathroom should be arranged so that no one except the nurse or attendant shall have access to them. The entire top floor, if possible, should be used. This separates the child from other members of the family, and removes him from the noises in the house. The room must be well ventilated and during warm weather the windows should be screened to exclude flies and other insects. All unnecessary rugs, furniture, hangings, pictures, etc., should be removed so as to facilitate proper cleansing of the room during and after the sickness.

A time-honored practice is to hang a sheet in the doorway saturated or sprayed with a disinfectant solution such as 5 per cent carbolic acid, or a 1:1,000 solution of bichlorid of mercury. This, of course, does not destroy the virus, as the disease is not spread through the air or by flying scales from the desquamation but it serves a useful purpose in reminding the attendants and other members of the family that a communicable disease is in their midst.

The attending physician should wear a washable gown which fastens around the neck and reaches the floor. He should put on a washable cap. On leaving the room after removing the gown and cap he should wash his hands and face and disinfect his stethoscope, auriscope and other instruments used in the sick room.

The nurse should wear wash dresses and a washable covering for her hair and should be quarantined with the patient and not mingle with other members of the household. She should gargle her throat and spray her nose with normal salt solution and should take her meals in the sick room or an anteroom, after disinfecting her hands, face and neck with a 50 per cent solution of alcohol.

The food for the sick room should be brought to the door and left for

the nurse to take in. All dishes and utensils as well as the bedclothing, etc., should be soaked in a 5 per cent carbolic acid or 1 : 1,000 bichlorid solution before being removed from the sick room.

The discharges from the nose, throat, ears and suppurating lymph-nodes should be collected on gauze or paper and immediately burned.

The duration of quarantine varies in different cases. It should continue as long as there is any discharge from the nose, throat, ears, mastoid or suppurating glands. The danger of infection comes from these discharges and not from the desquamation. The Sanitary Code of the New York State Department of Health defines the minimum period of isolation in scarlet fever to be "until thirty days after the development of the disease and until all discharges from the nose, ears and throat or suppurating glands have ceased." After the quarantine is raised the room should be thoroughly aired and cleansed. Sunlight, fresh air and soap and water are the best and most effective disinfectants. In many cities departments of health no longer fumigate or disinfect the sick rooms after scarlet fever, but insist on cleansing and airing the premises. The use of formalin or sulphur lamps gives a sense of false security which is very liable to lead to neglect in cleansing, washing and airing the rooms. The patient should receive a disinfecting bath of bichlorid 1 : 1,000 and his hair should be well shampooed and rinsed with the same solution. He should have his nose and throat sprayed with normal salt solution and should then be removed to another room and dressed in fresh clothing.

When there is any suspicion that the case was contracted through milk the sources of the milk supply should be investigated and all milk should be pasteurized.

The prevention of the spread of scarlet fever in the schools is an important and difficult problem. The simplest solution would seem to be to close the schools, but this is not feasible as it interferes with the education of the children without sufficient protection to warrant such a drastic procedure. It is practical, however, to close a class room for ten days in which a member has come down with scarlet fever and to treat as suspects all children who were in close contact with the child. When schools are closed the scholars, some of whom may already be infected, are more likely to mingle with others in various parts of the city and with younger children who do not go to school.

The test described by Dick and Dick in 1924 known as the Dick test furnishes a simple means of determining susceptibility to scarlet fever and gives rise to hopes that this disease can be controlled by early preventive methods and by immunizing susceptible children during an outbreak of scarlet fever. This test in its application and reaction is similar to the Schick test for susceptibility to diphtheria. The technic is also similar as

PLATE I.—THE DICK REACTION IN NORMAL PERSONS. (From Abraham Zingher, "The Dick Test and Active Immunization with Scarlet Fever Toxin," *Internat. Clin.*, 1924, J. B. Lippincott Co.)

A. Strongly positive (++) Dick reaction in normal child after one day.
B. Strongly positive (++) Dick reaction in normal child after two days.
C. Strongly positive (++) Dick reaction in normal child after seven days.
D. Strongly positive (++) Dick reaction in normal child after twenty-four hours.
E. Strongly positive (++) Dick reaction in normal child after forty-eight hours.
F. Positive (+) Dick reaction in normal child after twenty-four hours. To right is the faded pigmented spot of the positive reaction after seven days.
G. Positive (±) Dick reaction in normal child after twenty-four hours.

the required dilution of the scarlet fever toxin is introduced intradermally. The patient contracts a local attack of the disease after the injection which is confined to a small area around the point of injection. The toxin in proper dilutions to make the test can be procured from departments of health and commercial laboratories. The toxin used for the control test should be boiled for at least twenty minutes to avoid pseudoreactions. A positive reaction is indicated by a slight redness of the skin from two to three centimeters in diameter with slight swelling. It occurs in persons who have not had scarlet fever but who are susceptible to it. It is also present during the first few days of an attack of scarlet fever. This test has already proved very valuable in the control of scarlet fever in schools. The usual procedure during an epidemic is to give the Dick test to all the scholars and either remove or keep under observation those who show a positive reaction.

Active immunization was made possible by the work of Dick and Dick and is analogous in its technic to the injections of toxin-antitoxin for the active immunization against diphtheria. The injections of the diluted toxin are given intramuscularly in the triceps muscle. Three injections at intervals of one week are administered. A slight reaction both local and general may follow the first injection. The duration of the immunity is as yet unknown. The present consensus is that it lasts at least eighteen months and probably longer.

Passive immunization by doses of scarlet fever antitoxin is advocated by some authorities and decried by others. The immunity is only temporary and corresponds to that following a prophylactic injection of diphtheria antitoxin. The dangers are from the secondary serum sickness and severe reaction may result. Park feels that on account of these severe reactions and the fact that only about 10 per cent of exposed persons develop the disease the general use of this form of immunization is still open to question.

As a great amount of research work is being carried out in hospitals and laboratories in this country and Europe it is not improbable that in the near future the problem of immunization against scarlet fever will be solved.

General Treatment.—Confinement is necessary even in the mild type of scarlet fever. This should be for at least ten days for the mild and three weeks for the more severe cases in order to lessen the danger of post-scarlatinal nephritis. The patient should be in a sunny well-ventilated room, the temperature of which should not be over 60° to 65° F. There is no objection to a daily bath even during the eruptive stage, but this must be done with care to avoid any danger of chilling especially during the convalescent stage. It is a good plan to give a daily oil rub with carbolic acid 5 grains to one ounce of olive oil, as this will relieve the itching. Formerly it was used to disinfect the skin and prevent the scales from the skin from

getting into the air but this is not necessary as the scales have been found to be harmless. The throat, nose and ears should be carefully inspected each day and the urine examined every second day for at least three weeks. If there is a membrane on the tonsils a culture from the throat should be examined for diphtheria bacilli.

The diet should consist entirely of fluids during the first week or for as long as there is any fever. In some hospitals milk and water only are given in the first week. Water should be given frequently and in liberal quantities. When the temperature falls the diet can be increased to include soups, cereals, stewed fruits, toast and bread and butter. Nitrogenous foods should be avoided until the fourth week in order to relieve the kidneys. Eggs, therefore, are not advisable in any form until after the fourth week. There is no objection to orange or grapefruit juice. Rectal or forced feeding may be necessary when the child refuses to swallow on account of sore-throat.

The itching of the skin can be relieved by the carbolic oil rub above mentioned, or by a solution of bicarbonate of soda, one dram to a pint, or by the use of talcum powder.

A simple redness of the throat requires no special treatment. In the more severe forms of tonsillitis the throat should be swabbed as gargling is not efficacious even if the child is old enough to do it thoroughly. Peroxid of hydrogen diluted one-half and swabbed over the tonsils is useful in cleansing these throats. It can be followed by applying any one of the following: Mercurochrome 2 per cent solution; gentian violet 1 per cent solution; permanganate of potash 1 :40; nitrate of silver 2 to 4 per cent; argyrol 20 per cent; or a mixture of tincture of ferric chlorid 1 part, glycerin 1 part, water 2 parts. The external application of ice around the throat and the sucking of small pieces of ice help to relieve the pain and reduce the inflammation. In young as well as older children the use of a hot normal salt solution for douching the nostrils and throat is of decided benefit. Two or three quarts of hot normal saline solution in a douche bag are elevated about 2 feet above the patient's head. The end of the rubber tube is placed in one nostril and the fluid allowed to flow gently into the nose. This should be done in both nostrils and with the mouth open. The child soon gets used to this procedure and even welcomes it on account of the relief it affords.

The temperature does not require special treatment unless it produces general symptoms. A temperature of 104° F. for two or three days should not cause alarm. The fever is best reduced by hydrotherapeutic measures. If the temperature reaches 105° F., or over, cold packs give rapid relief. Sponging with cool water (85° F.) with alcohol is recommended. In

hyperpyrexia with cerebral symptoms the use of ice is indicated. Ice-caps applied to the head may quiet restlessness. Very young children object to cold applications or ice on the head.

Antipyretic drugs may be necessary to relieve not only the fever but the restlessness. Antipyrin, phenacetin and aspirin in small doses—1 grain for a child one year of age—are useful.

For the insomnia, allonal, amytal, etc., in 2-grain doses at night will give several hours sleep.

Stimulants may be necessary in cases in which there is cardiac weakness indicated by a weak, rapid, irregular heart and coldness and cyanosis of the hands and feet. Alcohol in the form of whisky or brandy is most valuable in these cases. Children in this condition can tolerate large doses, for example, with a child of two years give ½ to 1 ounce in twenty-four hours. Camphor oil given hypodermically is powerful and a rapid heart stimulant. Adrenalin hypodermically is of value in extreme cases. Caffein and digitalis are invaluable but their action is slower. Strychnin is a useful tonic and stimulant. A child of five years could take ⅙ grain of strychnin, 5 drops of the tincture of digitalis or ½ grain of caffein.

Treatment of Complications.—*Adenitis.*—The use of ice gives much relief and lessens the chances of suppuration. The ordinary rubber tonsillitis ice-bags filled with finely cracked ice can be readily applied around the neck with very slight discomfort to the child. Pigs' bladders can be used for this purpose. Painting the skin over the glands with iodin does not hasten their resolution but irritates and burns the skin. The use of iodex, mercurial ointment or ichthyol is of questionable benefit. These glands, even without ice or other treatment, will resolve without breaking down. When they soften and show evidence of pus the use of poultices and hot applications are indicated to hasten suppuration. An incision should not be made until the gland has thoroughly broken down so all the pus can be evacuated at the time of operation; otherwise the gland will discharge for some time and produce finally an ugly and disfiguring scar. In severe cases of cellulitis in septic cases prompt incisions should be made both in the gland and surrounding tissues without waiting for the formation of pus.

Ears.—Paracentesis should be performed at the first sign of bulging. Otitis is accompanied by pain and rise in temperature. When the internal ear is congested hot douches of boric acid (4 per cent) are of benefit. At least a quart of water as hot as can be borne should be used every two or three hours. After the irrigations two drops of the following prescription should be instilled in the congested ear.

℞ Phenol .... ℳii
Liq. Epineph. (1:1,000) ..... ʒi
Glycerin. .... ʒi

After incision of the drum of a spontaneous rupture the canal must be kept clean and clear. After the irrigations the canal is dried with sterile cotton swabs and a thin gauze ear wick inserted which should reach the bottom of the canal. The object is to keep the canal dry and sterile. As the gauze wicks become soiled, fresh ones are inserted.

There is always a danger of involvement of the mastoid cells in purulent otitis and when symptoms of mastoiditis appear prompt surgical procedures are indicated.

Nephritis.—A careful watch should be made throughout the attack for signs of kidney involvement, but no treatment is necessary for the simple albuminuria during the febrile period. True nephritis, one of the most dangerous complications of scarlet fever, usually does not appear until after the second week. Exposure to cold is claimed by some to be the active cause and all such exposure must be avoided during the course of the disease. Careful attention to the diet has already been mentioned. Urotropin in small doses is claimed by some to have value in preventing nephritis. When the urine is scanty and highly colored with albumin and casts, hot baths and compresses over the kidneys are useful in relieving the strain on the kidneys and promoting excretion from other organs. Acetate or citrate of potash may be given. The bowels should be made to move freely by saline laxatives and enemata. Only a mild diet should be offered and the child should be kept in bed. An account of the total amount of urine excreted as well as the fluid intake should be kept by the nurse. When the secretion becomes very scanty active measures should be taken to avoid uremia. High colon irrigations of hot water, dry or wet cups over the kidneys or prolonged hot baths may afford relief. Venesection or lumbar punctures are of value in relieving convulsions, and hypodermic injections of morphin and atropin are indicated in this condition. If there is much dropsy the fluid intake should be reduced. In the late stage when the nephritis becomes subacute or chronic, tonics are indicated. Basham's mixture is useful as it combines iron with a cathartic. The diet can be expanded at this time but salt should not be used if there is any edema. The anemia can be treated with tonics containing iron in some form.

Specific Treatment.—The close relationship between certain strains of streptococci and scarlet fever led many investigators to study methods of preparing antitoxins of various kinds. Paul Moser in 1902 in Vienna prepared a specific antitoxin from the blood of horses into which blood obtained from the heart of fatal cases of scarlet fever had been injected.

Moser isolated about thirty different strains of streptococci from the blood of scarlet fever patients, so his serum was polyvalent. He reported excellent results in the severe type of cases. No further attempt to produce an antitoxin was made until 1923 when Dochez obtained a serum by inject-

ing animals subcutaneously with agar containing the streptococci. Dick and Dick in 1924 injected sterile streptococcus filtrates into horses and later separated an antitoxin from their serum by the method of chemical precipitation used in the preparation of diphtheria antitoxin. The therapeutic action of the antitoxin is due to its capacity to neutralize scarlatinal toxin. Observations with this serum at the Willard Parker Hospital proved that it had antitoxin value but did not protect against secondary complications such as infected ears, kidneys, glands, etc.

The serum can be obtained from several commercial houses. Each unit represents the amount of antitoxin required to neutralize one hundred skin-test doses of toxin. The dosage depends on the size of the child and the severity of the attack. It is injected intramuscularly and intravenously but not subcutaneously. The earlier it is administered the greater is the benefit.

The following quotations from a circular prepared by the Division of Laboratories and Research of the New York State Department of Health is of interest in a discussion of the serum treatment of scarlet fever:

Antistreptococcus serum is prepared and tested in this laboratory. The value of the serum in the treatment of scarlet fever has been demonstrated. If administered early in the course of the disease it effects striking improvement even though the toxemia may be marked. Cases in which septic complications have already developed yield less readily to treatment. The general use of the serum for prophylaxis is open to question owing to the temporary nature of the passive immunity induced, the not infrequent occurrence of serum sickness and the possibility of inducing hypersusceptibility to later injections of horse serum. There may, however, be special circumstances in which its use as a preventive may be of value.

Distribution of Antistreptococcus Serum.—The serum is distributed for therapeutic use in 3000-unit packages, the volume contained in each package varying from 10 to 20 c.c. depending upon the antitoxic potency of the material. The antitoxic value of the serum is based on the neutralization of toxin as determined by intracutaneous tests on goats confirmed by similar tests on persons. According to the unit value adopted, which is that suggested at an informal conference in Washington in 1925, one unit of antitoxin neutralizes one hundred skin test doses of toxin.

Serum in packages containing 1500 units (5 to 10 c.c.) can be obtained from the State Laboratory on special request, for the passive immunization of persons whom the intracutaneous test has shown to be susceptible to scarlet fever.

Administration of Serum.—Early administration of the serum is essential. Usually one dose, if sufficiently large, is adequate. A second dose or even a third dose may be required if toxic symptoms recur. Satisfactory results are reported with intramuscular injections, but in severe cases intravenous injections may be preferable. For intravenous injection the dosage may be reduced.

A desensitizing, subcutaneous injection of from 0.2 to 0.4 c.c. of the serum should usually be given about two hours before the therapeutic dose; always, when the intravenous method is to be used. Under ordinary circumstances 3000 units of serum is usually sufficient. For very young children the doses

may be somewhat reduced. In extremely toxic cases it may be advisable to give for the initial dose from 6000 to 8000 units and to divide the dose giving part intravenously and the remainder intramuscularly.

The use of antitoxin should be reserved for cases of the severe or septic type as the serum reactions may cause more inconvenience and trouble than the disease itself. It is better to give one large dose, as repetition seems to have no effect.

PUBLIC HEALTH REGULATIONS

The attending physician is required by law to report promptly every case of scarlet fever to the health officer. When no physician is in attendance the head of the household must report at once to the health officer that the person is or may be affected with scarlet fever. A penalty may be imposed for neglecting to do this. If the child is attending school the principal should be notified so that the parents of other children who have been exposed may be informed. In some cities the health authorities permit other children in the family to be sent to live with adult friends during the period of isolation and to return to school after one week's observation, if well. If they remain at home even though they do not come in contact with the patient they must be excluded from school until one week after the quarantine is raised. The minimum period of isolation in New York State is thirty days after the development of the disease and until all discharges from the nose, ears and throat, or suppurating glands have ceased. Disinfection of all articles which have come in contact with the patient and of all articles soiled by the discharges from nose, throat, ears, bowels and kidneys is required by the health authorities. The sick room and premises must be thoroughly cleansed when the patient is released.

The résumé of the present status of scarlet fever as given by the Committee on Standard Regulations for the Control of Communicable Diseases follows:

1. INFECTIOUS AGENT.—*Streptococcus scarlatinæ.*

2. SOURCE OF INFECTION.—Discharges from the nose, throat, ears, abscesses or wound surfaces, and articles freshly soiled therewith. The nose and throat discharges of carriers may also spread the disease.

3. MODE OF TRANSMISSION.—Directly by personal contact with an infected person; indirectly by articles freshly soiled with discharges of an infected person, or through contaminated milk, or milk products.

4. INCUBATION PERIOD.—Two to seven days, usually three or four days.

5. PERIOD OF COMMUNICABILITY.—Three weeks from the onset of the disease, without regard to the stage or extent of desquamation, and only after all abnormal discharges have ceased and all open sores or wounds have healed.

6. METHODS OF CONTROL

   (*a*) The infected individual and his environment

      1. *Recognition of the Disease.*—By clinical symptoms.

      2. *Isolation.*—In home or hospital, maintained in each case until the end of the period of infectivity. If medical inspection is not available, isolation for twenty-eight days from onset.

      3. *Immunization.*—Exposed susceptibles as determined by the Dick test may be actively immunized by scarlet fever toxin.

      4. *Quarantine.*—Exclusion of exposed children and teachers from school, and food handlers from their work, until seven days have elapsed since last exposed to a recognized case.

      5. *Concurrent Disinfection.*—Of all articles which have been in contact with a patient and all articles soiled with discharges of the patient.

      6. *Terminal Disinfection.*—Thorough cleaning.

   (*b*) General measures

      1. Daily examination of exposed children and of other possibly exposed persons for a week after last exposure.

      2. Schools should not be closed where daily observation of the children by a physician or nurse can be provided for.

      3. In school and institutional outbreaks immunization of all exposed children with scarlet fever toxin may be advisable.

      4. Education as to special danger of exposing young children to those exhibiting acute catarrhal symptoms of any kind.

      5. Pasteurization of milk supply.

CHAPTER III

MEASLES

Definition.—Measles is a specific, highly communicable disease occurring in epidemics. It is more widely prevalent than any other eruptive fever and one to which human beings are universally susceptible, few persons reaching adult life without having contracted it. It is characterized by catarrhal symptoms of the eyes, nose and throat, fever and a typical eruption located on the mucous membranes and on the skin.

Synonym.—Rubeola, morbilli; la rougeole; Masern, Flecken; morbilli, rosalia; serempion.

HISTORY

While measles is perhaps the commonest infectious disease of childhood, yet very little was written about it by the ancient writers of medicine. The first description seems to have been made by Rhazes, an Arabian physician of the ninth century. He, in common with the medical opinion of that time, regarded measles as a variety of smallpox. In a chapter on the diagnosis of smallpox and measles, he says: "There is not in the measles so much pain in the back as in the Small Pox; nor in the Small Pox so much anxiety and naseau as in the Measles, unless the Small Pox be of a bad sort: and this shows that the Measles come from a very bilious blood."

Thomas Phaer, whom Ruhräh names "The Father of English Pediatrics," lived in the early part of the sixteenth century and also described smallpox and measles as the same disease, but referred to its recognition by the early Greek writers. A quotation from his book is of interest in this connection. "This disease is common and familier, called of ye grekes by the general name of exanthemata, and of plinie, papule et pitiute erupcinoes, notwithstanding ye cōsent of writers, hath obteined a distinctio of it in ii kindes; that is to saye, varioli the measles, and morbilli called of us the small pockes. They bee bothe of one nature, and procede of one cause, savinge that the small pockes of the inflammacion of bloude myugled with cholere." Nothing better or more to the point has been written by modern authorities than his remarks on treatment of measles. "The beste and most sure help in this case, is not to meddle with anye kynde of medicines, but to let nature worke her operacion, notwythestandynge yf they be to slowe in commyng oute."

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Sydenham, in the seventeenth century, was the first to claim that measles was a clinical entity and separate from smallpox.

Our modern conception of the disease from a clinical and epidemiological viewpoint dates from a series of investigations made by Panum in 1846 during an epidemic in the Faroe Islands where there had been no cases since an epidemic in 1781. Panum's work and conclusions were accepted by medical authorities and, in 1875, an epidemic, so severe and extensive as to cut off all communication with the outside world, broke out in the same islands and gave an excellent opportunity to observe the development and spread of measles.

ETIOLOGY

The specific cause or organism responsible for measles has not yet been identified so as to be universally accepted. A number of investigators have been able to produce measles experimentally by injecting blood of measles patients and also their nasal and buccal secretions into monkeys and have produced an identical disease with catarrhal respiratory and eruptive symptoms. Hektoen has been able to produce the same symptoms in human beings with similar injections of blood. Hermann advocates active immunization in very young infants by injecting the nasal mucous discharge of measles patients one to two days before the appearance of the eruption and claims favorable results.

It is of practical interest in this connection to note that in all of the experimental work the nasal and buccal secretions had to be taken two or three days before the appearance of the eruption and the blood injections eighteen to twenty-four hours before the eruption in order to be effective. In no instance were the attempts successful from material obtained two or more days after the eruption. All attempts to produce the disease by inoculation of desquamated scales have failed.

At the present time a vast amount of investigation concerning the etiology of measles is being carried on and it would seem that the confusion will soon be cleared. Many and various types of bacteria and protozoa have been obtained from the blood and nasal secretions by different observers and each has claimed their organism to be the essential cause of measles. Goldberger and Anderson discovered a filtrable virus which was capable of producing measles in monkeys. This was obtained from the blood and can only be found one day before the eruption. It resists drying and freezing for twenty-four hours and is destroyed by exposure to a temperature of 55° C. for fifteen minutes.

Tunnicliff describes a diplococcus which she found in the blood and nasal secretions during the preëruptive stage.

Ferry and Fisher claim to have isolated a streptococcus in pure culture

from the blood of patients in the early stages of measles. They call this organism *Streptococcus morbilli*. From these cultures they claim to have prepared a measles toxin and antitoxin which will give specific skin reactions in individuals who are not immune to measles, this reaction being absent in persons known to be immune to measles. Their description of this organism is as follows: "It is a medium sized, Gram-positive, aërobic streptococcus occurring in long chains in liquid medium and in chains of varying length on solid medium, which produces a small colony with a green halo on blood agar X X X. It is characterized by its production of an extracellular toxin specific to measles."

It now seems probable the *Streptococcus morbilli* and the Tunnicliff diplococcus are the same organism and different cultural methods are responsible for a few variations.

SUSCEPTIBILITY

Very young infants are relatively unsusceptible, especially if they are breast-fed. They become more susceptible after the sixth month and there is no infectious disease in which there is less natural immunity than in measles. Very few adults ever escape the disease unless they live in isolated rural sections. In the second Faroe Islands epidemic the only persons who escaped were those who had had measles during the first epidemic of sixty-five years before. It is possible for a person to pass through several exposures and later contract the disease. Holt records an epidemic in an institution where there were sixty-two children over two years of age. Five were protected by a previous attack and fifty-five of the remaining fifty-seven came down with the disease. In the same institution there were a number of young infants and although directly exposed not a single infant under six months of age came down with the disease.

It can be stated definitely that one attack of measles renders the individual immune to subsequent infection. There are exceptions to this statement but, while second attacks undoubtedly do occur, they are extremely rare. Patients and parents often report having had several attacks of measles but in some cases they must be considered as errors in diagnosis. The appearance of a rash with catarrhal conditions is not sufficient to make a positive diagnosis. The presence of the enanthem and Koplik's spots are necessary to make a diagnosis of measles.

Predisposition.—*Age.*—Measles is rare in young infants and babies under six months of age when exposed usually fail to contract the disease. There are authentic instances of measles in the newborn on record but they can be regarded as one of the curiosities of medicine (usually the mothers have measles at the time or soon after birth of the child). The largest number of cases appear between the first and sixth year of life. This is largely

due to the universal presence of the disease and general exposure and the immunity conferred by one attack. In the Faroe Islands epidemic where there had been no cases for sixty-five years all ages were equally affected. While young children are most susceptible yet persons of all ages who have never had measles may contract the disease.

Sex.—There seems to be no sex predisposition to measles and it attacks both sexes with equal frequency. The mortality statistics in New York State show that the death rate is higher among males than females (see Table IX, page 52).

Season.—Measles occurs in all seasons but is more common during the winter and spring months. The opening of the kindergartens and schools may account for the epidemics in October and the close contact in the schools is responsible for the frequency of cases during the winter and spring months.

Housing.—Measles is epidemic in the large cities where living conditions bring the population in close contact. The mortality rate is higher in the cities where crowded conditions prevail in the poorer districts. It was in Glasgow, for example, that the death rate was greatest where a family occupied one room, and least where over three rooms were occupied by a family. Isolated and rural communities may be free from the disease for many years but when it does occur it will attack all susceptible persons and a pandemic takes place. At the military camps in this country during the World War nearly all the cases of measles were in the country recruits, while only a few occurred among those from the large cities.

EPIDEMICS

Measles shows a tendency to appear in epidemics at certain intervals. Epidemics have appeared in New York City at intervals of two years for the past thirty years. This has been shown to occur in other parts of the country and in Europe.

The case fatality rate varies in different epidemics although there has been a distinct tendency for the mortality rate to fall during the past thirty years. The periodicity may be due to the disease having attacked all susceptible children in the community, burning itself out and recurring when a fresh supply of susceptibles are available. When the epidemics are widely separated, as for instance in the Faroe Islands, the disease attacks both young and old and the mortality is high. It is very doubtful if it is desirable to increase the intervals between epidemics over a maximum of five years.

It is most desirable and necessary to prevent the disease from attacking children under three years of age.

PATHOLOGY

Measles has no characteristic pathologic changes with the exception of the eruption on the skin and mucous membranes. The fatal cases are the result of complications and sequelæ. The appearance of the skin is the result of a superficial inflammation with round-cell infiltration about its hair-follicles, sweat-glands, sebaceous glands and capillaries. The swelling, which is most marked on the face, is due to edema and exudation characteristic of inflammation. This infiltration causes the papular elevation so characteristic of the eruption of measles. These skin lesions are not present after death unless hemorrhages have taken place and left a staining and a mottled appearance of the skin. After the eruption has faded the superficial layer of the epidermis will desquamate in fine branny scales and the exudate is absorbed.

The mucous membranes are involved in a similar manner as the skin. The conjunctivæ, nasal, pharyngeal, laryngeal, tracheal and bronchial mucous membranes show a catarrhal inflammation which varies in intensity with the severity of the infection. The submucosa is more deeply involved than in other infectious catarrhs and the extravascular infiltration is greater. The buccal mucous membrane shows small areas of fatty degenerations which were described by Koplik and bear his name.

The catarrhal inflammation extends down to the alveoli of the lungs, in severe cases causing bronchopneumonia.

The lesion in the pharynx may become membranous in severe cases instead of catarrhal.

The lymphatic glands are involved in the severe cases and the superficial lymph-nodes are palpable and the lymphoid tissue of the nasopharynx and intestinal tract are swollen.

The spleen is often slightly enlarged as the result of congestion. The liver may show focal necroses. The heart may present inflammatory changes involving the endocardium. The kidneys are not so frequently involved as in scarlet fever.

The bacteria found in the respiratory lesions are staphylococci, pneumococci and influenza bacilli, usually in association, rarely one variety alone.

The condition in the lungs and lymph-nodes seems to be favorable for the development of tuberculosis.

SYMPTOMS

Period of Incubation.—This embraces the interval between the initial infection and the appearance of fever and catarrhal symptoms. There are no objective or subjective symptoms during this period. Hermann found

a definite loss of weight during the latter part of this period. In ninety-six children over eight months of age he found an average loss of over 5 ounces, while in thirty-three infants under eight months there was an average gain of 2 ounces. He explains this on the ground that the course of the disease is much milder in young infants and their appetite and sleep are not so greatly disturbed.

The length of this period averages between eleven and fourteen days. Hermann found it was between nine and twelve days in 82 per cent of the cases.

In 144 cases studied by Holt when the period of incubation could be definitely traced it was:

Days	Cases
Under 9	3
9-10	22
11-14	95
15-17	19
18-21	5

These figures coincide with those obtained by other authors. Hektoen observed in cases experimentally produced in human beings that the average interval between inoculation and the initial rise of temperature was seven or eight days. In monkeys this period averages eleven days. The time between the exposure and the appearance of the rash can be stated as two weeks in the great majority of cases.

Period of Invasion.—This is sometimes called the catarrhal stage or the prodromal period. It extends from the initial rise in temperature and the appearance of the characteristic eruption.

The fever is the first and most frequent symptom. The onset is apt to be slow and insidious and the temperature may have to be taken every four hours in order to detect it. It usually rises to 100° or 101° on the first day. In a majority of the cases it gradually increases each day until 104° or 105° is reached with the appearance of the eruption. In other cases it may rise the first day to 102° and then fall to normal for a couple of days, with an abrupt rise to 104° or over when the rash appears. It may remain about 100° or even be unnoticed until the appearance of the rash. The temperature curve in a normal uncomplicated case presents a gradual rise with morning remissions until the rash breaks out and then an abrupt fall. Instead of a fall by crisis there may be a slower descent and a fall by lysis.

Hyperpyrexia as high as 110° F. has been reported. The temperature lasts on an average one week.

Catarrhal symptoms of the mucous membranes of the upper respiratory tract are characteristic of the period of invasion. The eyes become con-

gested and watery. There is marked photophobia and a tendency for the lids to stick together. The caruncle at the inner canthus of the eyes is swollen and red, and small bluish-white spots are frequently observed. Sneezing is frequent and is accompanied with a mucopurulent nasal discharge. There is a dry, harsh cough which may be incessant and the voice is hoarse as a result of the catarrhal condition of the throat and larynx. The face, especially about the eyes, becomes swollen and puffy and the child appears to have an acute coryza.

The tonsils and pharynx are swollen and there is frequently some pain on swallowing which may have something to do with the loss of appetite. The peritonsillar lymph-nodes are enlarged and tender. The lymphoid tissue on each side of the uvula is often swollen.

Hermann has described a condition of the tonsils which he considers typical of measles and found in about half of the cases. The tonsillar spots as he describes them are spots or streaks which vary in size, number, shape and color. There may be only two or three or a large number. The color depends on the thickness of the exudate and varies from a grayish blue to a white. They vary in size from the point to the head of a pin. They are seen only in the early stage of invasion and disappear after twenty-four to forty-eight hours. They usually appear before the Koplik spots. He calls them "tonsillar spots."

The appearance of the rash on the mucous membranes is termed "enanthem," and this is one of the most important diagnostic points. This enanthem is caused by the same virus which is responsible for the changes on the skin. The enanthem appears before the exanthem, probably on account of the greater blood supply and the character of the tissues. The mucous membrane of the mouth is involved several days before eruption. The hard palate shows very early in the stage of invasion a number of small and irregular bright red spots which are slightly raised above the level of the mucous membrane. They vary in size from the head of a pin to the head of a pencil. They are also seen on the mucous membranes of the cheeks, especially about the angle of the jaws. Not infrequently small hemorrhagic spots appear on the hard palate.

Koplik's Spots.—These are different from the enanthem and consist of bluish-white specks on a red base seen on the mucous membrane of the cheeks most frequently opposite the upper molars and on the inside of the lips. They are found one to four days before the eruption on the skin. The original description by Koplik is as follows: "If we look in the mouth at this period (of invasion), we see a redness of the fauces; perhaps not in all cases, a few spots on the soft palate. On the buccal mucous membrane and inside the lips we invariably see a distinct eruption which consists of small red spots of a bright red color. In the center of each spot there is

noted, in strong daylight, a minute, bluish-white speck. These red spots, with accompanying specks of a bluish-white color, are absolutely pathognomonic of beginning measles and when seen can be relied upon as a forerunner of the eruption. No one has to my knowledge called attention to the pathognomonic nature of these small white spots. Sometimes only a few red spots with this central bluish point may exist, six or more; in marked cases they may cover the whole inside of the buccal mucous membrane. . . . The eruption just described is of greatest value at the very onset of the disease—the invasion. As the skin eruption begins to appear and spreads, the eruption on the mucous membrane becomes diffuse and the characters of the discrete eruption disappear and lose themselves in an intense general redness."

These spots can be seen on careful observation in over 90 per cent of all cases of measles and are now generally accepted as pathogenic of the disease. They are never seen in other conditions. They vary in number from two or three to an innumerable number. A strong light, preferably direct sunlight, is necessary to detect them. The mouth should be opened widely and the cheek pressed out with a spoon or tongue stick. They must be differentiated from trauma of the mucous membrane, stomatitis, food débris and air bubbles.

Koplik's spots disappear when the skin eruption is at its height. The gums are usually reddened and slightly swollen and are frequently covered with a bluish-white deposit which gives them the appearance of having been touched with a silver nitrate solution. It may cover a large area of the gums or only a small portion.

Preëruptive Rashes.—These are not infrequent and may be misleading, so the possibility of such rashes must be borne in mind so as to avoid errors in diagnosis. They may appear as early as the first day of the stage of the invasion. The types most commonly seen are scarlatiniform, urticaria or erythematous. They will be discussed more fully under diagnosis.

The Blood.—There is a moderate leukocytosis in the latter part of the period of incubation, which is followed by a leukopenia during the invasion and eruptive stage. A daily leukocyte count may be of diagnostic value. Hecker found that there is a reduction in the relative percentage of the lymphocytes as early as six days before the appearance of the rash.

When a decided leukocytosis is found after the eruption it may indicate some complication.

The constitutional symptoms during this period, besides the fever which has been described, are headache, drowsiness, pains in the back and legs. Diarrhea is uncommon and constipation is the rule. Vomiting is not the rule, although it may be troublesome in children who have a tendency to

acidosis. Severe epistaxis occurs in a small percentage of cases. The onset may be very mild and may be unrecognized until the rash appears. The mild cases are most frequently seen in infants and young children.

The duration of this period varies from one to ten days but is usually from three to four days. It is shorter the younger the child.

Holt studied 270 cases and found the stage of invasion, *i. e.*, from the beginning of the catarrh until the appearance of the rash, as follows:

Days	Cases
1 or less	35
2	47
3	64
4	64
5	29
6	20
7	6
8	2
9	2
10	1

Period of Eruption.—*The Exanthem.*—About the time of the appearance of the eruption the child becomes apathetic, wants to be left undisturbed and takes no interest in his surroundings. The temperature is high with a corresponding increase in the pulse and respiration. The catarrhal symptoms increase, especially the conjunctivitis and coryza. There is no appetite and if food is forced it will be vomited. The tongue is coated and the breath is foul. The tongue may show areas of redness and the papillæ may be prominent, giving it an appearance similar to that observed in scarlet fever. The laryngitis becomes more severe and the cough more persistent and troublesome. Not infrequently a diffuse bronchitis develops.

The eruption is first seen on the face, back of the ears, at the border of the hair, on the cheeks and around the mouth and nose. It shows a predilection for the face where it after becomes confluent and accompanied by a marked swelling, making a marked change in the appearance of the patient. It extends over the neck and down the back and trunk and then the arms. The palms of the hands may show a marked rash before it appears on the back of the hands and arms. The thighs and legs are last affected. It fades in about the same order as its appearance. It reaches its full development in two to three days and disappears in from three to five days, according to its intensity, and may leave a pigmentation behind which may take two weeks or more to disappear. The rash appears first as small, darkish red macules which are slightly elevated and look like fleabites. They vary in size from that of a pinhead to a bean, and are oval, round or irregular in

shape. They frequently coalesce and become confluent, especially over the face, and on the body assume crescent-shaped form with healthy skin in the center. The margin is usually sharply defined and the raised edges are palpable and the surface has a velvety feel. During the first twenty-four hours the skin lesions increase rapidly in number. They disappear on deep pressure unless small hemorrhages have taken place in and about the lesion. This may occur in cases of no great severity and the hemorrhagic form does not necessarily imply a bad prognosis.

The eruption fades from the face after twenty-four hours and slowly disappears about the time it is at its highest development on the extremities. It often leaves a brownish discoloration which remains for about a week and is valuable in diagnosis even after the acute attack has subsided. In hemorrhagic measles the blood stains pass through the sequence of colors seen in extravasated blood. Holt found the hemorrhagic type in about 5 per cent of his cases. This is the form spoken of by the older writers as "black measles." Hemorrhages may take place from the mucous membranes, especially of the nose, stomach and urinary tract. The measles assume a port wine color and do not disappear on pressure. This type of eruption is more frequent on the body and forearms.

Measles with a hemorrhagic rash must not be confused with the hemorrhagic type just described.

The rash often presents many variations from the typical textbook description. It may be very faint and show little elevation and only last one or two days. This is the usual type in very young and nursing infants and in weak, debilitated children. It may also consist of minute spots which closely resemble the rash of scarlet fever. Papular and vesicular forms of the rash may occur. This is most frequent over the chest and back in the parts where the sweating is more profuse.

The rash may fade before it has fully developed or take on a cyanotic hue. This is due to some circulatory disturbance and may be the onset of a pulmonary complication or profound toxemia. With an improvement in the heart action and the peripheral circulation the rash will reappear. This "striking in" of the rash is viewed with alarm by the laity. The first appearance of the rash may be on some parts of the body, not the face, and later spread over the body and face. Hermann reports having seen a recurrence of the eruption a week after the original eruption. Recurrences may be considered reinfections similar to relapses in typhoid fever and are accompanied with a new rise of temperature.

There is a fine branlike desquamation which begins as soon as the rash has subsided and is first noticed on the face and neck. It never appears as large flakes or scales as in scarlet fever, and is often so slight as to escape

notice. It is most marked in cases in which there has been a profuse eruption and usually lasts about a week. No one has been able to demonstrate that this desquamation is infectious or contains the virus. During desquamation the patient feels quite well although the cough may be troublesome and the eyes remain sensitive to light. A distinct and characteristic odor can be noticed in a number of cases at the height of the eruption.

The lymph-nodes are usually slightly enlarged in this stage, especially those of the axilla and the cervical and inguinal regions.

The urine is highly colored and scanty and shows a high specific gravity. Albumin is present in severe cases with a high temperature. Evidence of acidosis—diacetic acid and acetone—is quite frequent and the diazo-reaction is positive. These changes may be present in other infectious diseases and are not significant of measles alone.

The stages of eruption and desquamation average about a week or ten days in duration. The patient feels so well after the rash disappears that it is difficult to keep him under control. Care has to be taken to avoid taking cold, as the child is more susceptible to respiratory infections.

CLINICAL VARIETIES

Mild Form.—This is seen in infants less than five months of age. The fever is never high and the catarrhal symptoms are slight and may be absent. The rash is discrete and never confluent, and the duration is short. This type of the disease is now frequently observed in children to whom convalescent blood-serum has been administered, and is called a modified type of measles. Hermann found a much longer period of incubation in these cases which he attributes to diminished susceptibility on the part of young infants and inoculated children.

The diagnosis in these cases is difficult without the presence of an epidemic or the history of exposure or of inoculation.

Moderate Form.—This form presents the usual type of the disease with the gradual onset, catarrhal symptoms and fever. It is usually found in children over three years of age. The entire duration is usually about a week.

Severe Form.—The age and condition of the child influence the severity of the disease. It may start in as a mild form and on account of the previous state of health, unhygienic surroundings, improper treatment, etc., it may become serious and assume septic form. The fatality rate of the infection varies in different epidemics and in different localities. It may appear as an overwhelming infection from the start. In remote and isolated regions where the disease has not appeared in many years it is apt to be very severe with a high mortality.

COMPLICATIONS AND SEQUELÆ

The most frequent and most important complication of measles is the involvement of the respiratory tract. Bronchopneumonia is the cause of almost all of the deaths that occur in measles. The frequency and mortality from pneumonia are greater in children under three years of age. It occurs more frequently among children in institutions than in private homes. Holt reports that bronchopneumonia occurred in about 40 per cent of three hundred children affected in two institution epidemics and 70 per cent of those who had pneumonia died. It is more common in the winter months and usually appears when the eruption is at its height or just commencing to fade.

Bronchopneumonia is more apt to develop in children who are bundled up during the period of invasion in superheated, darkened and unventilated rooms, which are deemed necessary by many ignorant persons to "bring out" the rash.

Lobar pneumonia is less common and found usually in older children and may be followed by empyema.

Pneumonia is to be suspected if the temperature continues high after the full appearance of the rash.

Bronchitis is present in nearly all the cases. It is not dangerous unless it extends to the smaller bronchi and causes a capillary bronchitis which is indistinguishable from bronchopneumonia. Tuberculosis is not an uncommon sequela of measles among children who have latent tuberculous processes or live in a tuberculosis environment. In young children this occurs in the form of tuberculous adenitis, miliary tuberculosis or tuberculous meningitis. Von Pirquet observed that in such cases where the skin reaction had been positive it became negative.

The Larynx.—Catarrhal laryngitis accompanies almost all of the cases, especially in children who are subject to croup. Membranous croup is a cause of a small percentage of deaths among institutional cases. The membrane may be due to a streptococcus infection. True Klebs-Löffler infection may occur and is a very serious complication. In an institution epidemic of sixty-five children a fatal streptococcus membranous croup occurred in seven children.

Throat.—Inflammation and redness of the throat are as characteristic of the disease as the eruption on the skin. The tonsils, uvula, palate and pharynx are swollen and congested. The tonsillar crypts show a white exudate in a small proportion of the cases. True diphtheria may occur but the membrane is characteristic. The throat symptoms are not as severe as in scarlet fever but in severe cases associated with streptococcus infection they may cause death from general sepsis.

Mouth.—The gums are not infrequently inflamed and in children who are below par or confined in institutions an ulcerative stomatitis may develop. This is more apt to occur in children with carious teeth and when the resistance is low the ulcerative process progresses and a gangrenous stomatitis may result. A number of cases of noma of the cheeks have been reported as a complication of measles occurring in institutions. In an outbreak in the Albany Orphan Asylum four cases of noma of the cheek occurred and in two the vulva was involved. The Klebs-Löffler bacilli, Vincent's bacilli and the spirochetes have all been found in gangrenous stomatitis. This is nearly always fatal.

Digestive System.—Active vomiting accompanies many cases of measles, especially in the preëruptive stage. This is often accompanied with acetone and diacetic acid in the urine.

Diarrhea is very frequent and is more common in certain epidemics and during the summer months. There may be severe abdominal pain and the stools are blood-tinged and filled with mucus. These symptoms appear at the height of the eruption and may last for two or three weeks. Cases of ileocolitis may in the summer months show a higher mortality than the pulmonary complications.

Nose.—The swelling of the mucous membrane of the nose interferes with breathing in young infants and makes nursing and bottle feeding difficult. There may be a copious nasal discharge which may cause excoriation or even eczema of the upper lip. Cases of diphtheritic rhinitis have been reported.

Ears.—The inflammation of the nasopharynx not infrequently extends to the middle ear through the eustachian tubes. The temperature rises and the child suffers a great deal of pain and loses sleep and appetite. The frequency varies in different epidemics and occurs in from 1 to 15 per cent of the cases. Both ears are generally involved and a few cases develop mastoid. The ear-drums are congested and there is a slight bulging. If it is a simple catarrhal inflammation it may disappear spontaneously. If the fever persists a paracentesis should be done at once which will give immediate relief.

Kidneys.—Albumin is present in the urine in cases of moderate severity with a high temperature. True nephritis is rare in contradistinction to its frequency after scarlet fever. A few cases have been reported in the literature.

Heart.—The heart is rarely affected although cases of endocarditis and pericarditis have been reported. When it does occur it may leave a permanent lesion of one of the valves. Myocarditis is an accompaniment of septic infections.

Skin.—An obstinate eczema may be associated with measles although previous chronic eczema or psoriasis may show a temporary improvement during an attack of measles. Impetigo, herpes facialis and urticaria are sometimes associated with the measles rash and in children who are in poor physical condition furunculosis may develop. Small nodules of a reddish-brown color with a necrotic center covered with a scale called tuberculides are occasionally seen in children with tuberculosis.

Nervous System.—Delirium occurs in children with high temperatures or a severe infection and in nervous and neurotic children. It has no special significance. Convulsions at the onset are rare but later on they are more common in connection with a high fever. They are present when complications associated with bronchopneumonia, otitis and meningitis affect very young children. It is not at all uncommon during the height of the disease for the children to be dull and apathetic.

Meningitis due to the tubercle bacillus, pneumococcus and meningococcus have been observed. Acute encephalitis has developed as a sequela of measles.

Mental disturbances occasionally follow an attack of measles but are usually of a temporary character.

Association with Other Diseases.—Measles may be complicated by diphtheria, which makes the condition more serious, especially if it involves the larynx. This occurs more frequently among institutional children. Whooping-cough is a much more frequent complication and epidemics of measles and whooping-cough may occur together or follow each other. This is a dangerous combination as both diseases have a tendency to affect the respiratory tract.

When scarlet fever and measles occur together the diagnosis may be difficult as scarlatiniform prodromal rashes in measles are not uncommon. The characteristic symptoms of each must be present, for the course of each disease is not interfered with.

Measles and chickenpox may occur at the same time.

Comby reported that of twenty-three children in whom whooping-cough followed measles the mortality was 43 per cent, of fifteen where scarlet fever followed measles 33 per cent died, and of fifteen in whom diphtheria followed measles there was a mortality of 13 per cent.

There seems to be a close relationship between measles and tuberculosis. In children with a latent tuberculosis or who are in a pretuberculous stage, measles may activate the process. Miliary or pulmonary tuberculosis may follow an attack of measles. Tuberculous adenitis, especially of the cervical lymph-nodes, may develop and tuberculosis of the joints and bones may appear as a late development. Von Pirquet found that the skin tuberculin test which had been positive becomes negative during an attack of measles.

DIAGNOSIS

It is not possible to diagnose measles or any of the eruptive diseases of childhood by the appearance of the rash alone. It is now universally accepted that measles cannot be present unless the characteristic changes in the mouth are present. Koplik's spots are present in over 90 per cent of the cases and are found in no other condition. The enanthem over the palate and mucous membrane of the mouth, the appearance of the gums and tonsils taken in conjunction with the Koplik's spots make the diagnosis certain. The presence of an epidemic and a history of possible exposure ten to fourteen days previous are helpful in making diagnosis.

Differential Diagnosis.—*Scarlet Fever.*—This may be difficult without a history of exposure during the period of invasion. Measles may be ushered in by vomiting and fever and a roseola similar to scarlet fever may appear. This rash is not so marked over the face, and the white skin surrounding the mouth is not in evidence. The tongue may show in measles a striking similarity to that of scarlet fever. The pulse in measles is not so rapid and the Koplik's spots and the macular enanthem over the palate and mucous membrane of the mouth are never present in scarlet fever. The catarrhal symptoms and cough are distinctive of measles. The blood-picture is different. After a few days the typical morbilliform rash appears. Measles will attack practically all susceptible children who come in contact with a case, while scarlet fever only infects about 25 per cent who are exposed.

German Measles.—For many years rubella and measles were considered the same disease. The differential diagnosis may be difficult if the child is seen first in the stage of eruption or if it is a very mild or modified type of measles. The appearances in the mouth are absent in German measles and the fever and catarrhal symptoms are less marked. The rash in German measles is more discrete and more pink in color and the chain of enlarged lymph-nodes appears earlier and is more marked than in measles. The presence of typical measles in the family or close associates is of assistance in reaching a diagnosis.

Influenza.—In the stage of invasion there is a great similarity in the catarrhal symptoms, but with the appearance of the mouth, the presence of Koplik's spots and the breaking out of the characteristic rash the diagnosis will be plain.

Skin Diseases.—The constitutional subjective symptoms of measles and the characteristic changes in the mouth are absent in skin lesions which bear an objective similarity to the rash of measles. Skin rashes of intestinal origin are often mistaken for measles, especially in infants, but the other signs of the disease must be present in order to make a diagnosis.

Antitoxin and Drug Rashes.—The urticaria following the injection of serum may present the appearance of measles. A measles-like rash occasionally follows vaccination. An eruption like that of measles may follow the use of drugs in certain individuals. Those most likely to produce such a rash are antipyrin, quinin, chloral, iodids and cubebs. In these cases the absence of catarrhal and oral symptoms and the history of the case make the diagnosis simple.

PROGNOSIS

Many factors enter into the problem of prognosis. It is generally admitted that the morbidity figures are inaccurate, as a very large percentage of cases are not reported or recorded. The mortality records are more reliable although fatal cases may be reported as pneumonia which were primarily caused by measles. The principal factors are the age of the patient, the season of the year, the previous physical condition of the patient, the housing and hygienic conditions, the character of the epidemic, whether the cases are treated at home or in an institution and whether it occurs in the country districts or in large cities.

The general death rate based on 100,000 population in the United States death registration area, in New York State, in New York City and in the State of New York exclusive of the City of New York is shown in the following table prepared under the direction of DePorte of the New York State Department of Health.

TABLE V.—DEATH RATE FROM MEASLES PER 100,000 POPULATION IN UNITED STATES DEATH REGISTRATION AREA, NEW YORK STATE, 1915-1925

Year	United States Registration Area	New York State	New York City	New York State Exclusive of New York City
1915	5.4	8.5	12.1	4.6
1916	11.1	9.3	9.2	9.3
1917	14.3	8.9	10.4	7.3
1918	10.8	12.5	14.4	10.4
1919	3.9	3.4	3.9	2.9
1920	8.8	10.5	13.0	7.6
1921	4.3	3.9	2.9	5.0
1922	4.3	10.7	17.0	3.4
1923	10.8	6.0	4.2	8.1
1924	...	6.7	8.7	4.5
1925	...	2.5	2.2	2.9

The death rate of measles in the United States registration area varies from 3.9 to 14.3 per 100,000 population. The mortality varies in different years and the highest point occurred in 1917 in the registration area, in 1918

in New York State and in 1922 in New York City. It is interesting to note that the mortality rate is higher in New York State every other year.

In terms of per cent it appears that measles is responsible for less than 1 per cent of all deaths in the United States.

The rural and urban death rates were separated in New York State for the years 1924 and 1925, as shown in the following:

DEATH RATE FOR MEASLES PER 100,000 POPULATION IN NEW YORK STATE

Year	Rural	Urban
1924	4.1	4.8
1925	1.4	3.9

The higher rate in the cities cannot be due to a more virulent infection but is no doubt influenced by the crowded and unhygienic surroundings with a great tendency to pneumonia. The ages of those attacked is lower.

Holt gives the following table of the mortality from measles in an institution for children:

AGE	CASES	MORTALITY, Per Cent
6-12 months	42	33
1-2 years	51	50
2-3 years	27	30
3-4 years	20	14

The effect of the season of the year is shown in the following table which shows the largest number of deaths occurred in the months of March, April and May and the lowest mortality in the summer and fall months. The reported morbidity is even lower proportionately. Some of the most fatal institution outbreaks have occurred in the summer. This table also shows the jump in mortality every other year.

TABLE VI.—MORTALITY FROM MEASLES IN NEW YORK STATE PER 100,000 POPULATION FROM 1915 TO 1925 ACCORDING TO MONTHS

Year	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1915	3.0	3.7	7.2	15.0	18.4	20.9	11.4	6.1	3.9	3.0	4.4	6.1
1916	8.7	12.5	16.4	20.3	19.5	10.6	9.8	4.7	2.2	1.8	1.3	3.5
1917	8.1	11.7	8.6	14.1	17.0	18.0	11.5	4.4	2.8	1.5	2.3	7.4
1918	13.9	19.1	29.1	31.2	21.9	15.5	8.4	4.3	2.5	2.6	1.2	1.3
1919	2.1	2.1	3.0	5.7	7.2	3.8	2.5	1.3	.8	1.0	2.8	8.9
1920	14.9	27.2	18.2	21.4	15.4	9.3	5.2	2.6	1.4	2.3	3.6	5.9
1921	8.0	9.5	7.5	4.8	4.7	4.6	3.0	1.2	.3	.4	1.3	2.8
1922	6.9	12.7	20.4	28.1	30.9	17.7	4.8	2.1	.5	.5	1.1	2.8
1923	4.0	4.8	5.6	9.9	14.6	11.6	7.1	2.7	.8	.9	3.8	6.4
1924	8.6	9.7	17.3	19.1	13.2	8.0	2.5	.7	.4	.3	.2	.7
1925	.4	.9	1.5	2.9	4.4	5.6	3.1	1.2	1.0	.5	2.9	5.7

Age is an important factor in the prognosis. The great majority of deaths occur in children under three years of age. After that age the deaths from measles are very few. The serious complications, especially that of bronchopneumonia, are rare in children over four years of age. The following table gives the death rate for measles per 100,000 population in New York State for the ten-year period, 1915 to 1924. It shows the total reported deaths for all ages as well as by year periods, the mortality rate per 100,000 deaths of these cases and also the percentage rate of all causes by age groups.

TABLE VII.—DEATH RATE IN MEASLES PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1924, ACCORDING TO AGE

Age, Years	Number		Rate		Per Cent of All Cases	
	1915	1924	1915	1924	1915	1924
Under 1.............	204	197	84.0	84.2	.8	1.2
1	365	295	196.1	138.0	6.9	9.6
2	125	106	63.1	48.3	6.1	7.0
3	49	43	25.2	19.5	3.8	4.7
4	20	15	10.7	7.0	2.2	1.9
5-9	48	54	5.4	5.1	1.8	2.1
10-14	10	3	1.2	.3	.6	.2
15 and over	23	28	.3	.4	.02	.02
TOTAL ALL AGES ..	844	741	8.5	6.7	.6	.5

While the morbidity statistics are not entirely reliable yet they are of interest. Table VIII shows the reported number of cases of measles per 100,000 population in the State of New York by months and by years. By comparing this with Table VI it will be seen that the number of cases are greater every other year and correspond with the higher mortality rates of the same year. By far the largest number of cases are reported in the winter and spring months.

TABLE VIII.—MORBIDITY FROM MEASLES IN NEW YORK STATE PER 100,000 POPULATION FROM 1915 TO 1925, ACCORDING TO MONTHS

Year	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1915.....	308.3	465.3	798.7	1272.3	1466.5	1336.5	507.7	148.5	75.3	155.8	415.7	638.3
1916.....	756.0	925.3	1201.4	1432.5	1414.6	1166.0	614.5	126.5	42.0	46.8	118.8	216.0
1917.....	394.3	645.1	918.9	1136.4	1362.0	1149.8	420.0	110.9	63.1	118.4	271.0	636.2
1918.....	893.9	1092.7	1572.3	1765.2	1658.1	911.7	554.0	153.0	54.3	67.4	51.2	40.6
1919.....	80.4	117.7	164.8	243.2	350.5	267.3	141.3	49.2	25.9	74.4	186.6	598.7
1920.....	1234.2	1354.4	1215.1	1229.2	1243.9	1056.4	466.5	134.4	59.2	137.0	372.2	534.5
1921.....	737.2	819.3	694.0	574.9	597.0	443.8	173.0	60.5	31.7	34.2	85.8	168.1
1922.....	315.0	708.3	1090.5	1378.6	1468.0	843.1	323.0	66.4	29.3	50.7	87.1	199.1
1923.....	400.1	525.0	679.0	874.5	1477.7	1369.5	526.0	125.8	70.1	181.2	371.9	521.7
1924.....	829.1	1138.5	1610.0	1587.1	1144.1	781.5	289.0	56.2	22.2	53.0	60.9	99.0
1925.....	107.7	184.1	276.9	354.7	387.2	414.7	147.5	49.4	31.4	122.6	327.5	770.2

The influence of sex in the mortality from measles is very slight although the mortality is slightly greater among the males. This is shown in the following table:

TABLE IX.—DEATH RATE IN MEASLES PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1924, ACCORDING TO SEX

Year	Male	Female
1915	9.9	7.7
1916	9.9	8.8
1917	9.4	8.6
1918	13.2	12.0
1919	3.5	3.4
1920	11.0	10.0
1921	3.9	3.9
1922	11.3	10.1
1923	6.3	5.8
1924	7.1	6.4

The presence of complications, especially on the part of the respiratory system, renders the prognosis more unfavorable. Cases in which the eruption is cyanotic in color are indistinct and slow in appearance; the prognosis is not so good as such cases are often associated with disturbance of the heart or lungs. The height of the temperature has a bearing on the prognosis as is shown in the following table from Holt, showing the height of temperature and the mortality in 161 hospital cases:

HIGHEST TEMPERATURE, Degrees Fahrenheit	CASES	MORTALITY, Per Cent
Not over 102	6	0
102.2-103.5	14	7
104 -104.4	49	16
105 -105.5	65	40
106 and over	27	80

TREATMENT

Prophylaxis.—Measles is such a common disease that with the laity at least familiarity breeds contempt. They have come to look upon it as such a mild disease that its prevention is considered of slight importance; as every child will contract it sooner or later the sooner it is over the better. It is seldom justifiable to expose children unnecessarily to measles. It is the duty of every physician to prevent disease both in the interest of his patient and as a measure of public health and to employ every means to this end. While measles rarely seriously affects strong robust children, yet in infants, young children and delicate children it may and often is

serious and even fatal and every possible means should be employed to protect them from infection.

This is especially true with children in institutions and those predisposed to tuberculosis.

The extreme contagiousness for several days before the appearance of the eruption and in many cases before a diagnosis is made, the lack of precise knowledge of the infective agent and the almost universal susceptibility all tend to make the problem of prevention more difficult to solve. The chief measures employed at the present time are: (1) Isolation of both suspected and active cases, (2) quarantine of exposed susceptible children, and (3) protective inoculation of exposed children.

Isolation in the Home.—When a child comes down with measles he should be confined in a room from which other members of the family can be excluded. No one but those actually nursing and caring for the child should be allowed to enter this room. If possible, the sick room should be on the top floor. Strict isolation is not necessary after the rash has disappeared and the temperature has been normal for a couple of days. This is usually about five days. Such isolation is also of great benefit to the patient as it will greatly lessen any chances of his being infected with bacteria such as pneumococci, streptococci, etc., which would be apt to produce dangerous complications in his weakened condition. All cases should be reported at once to the health officer so that exposed children can be traced and watched. A placard on the door, especially in the tenement districts of cities, warns other persons of the presence of the disease and perhaps prevents other children from coming in contact with the children of the affected family. The study of measles in monkeys has shown that measles cannot be transmitted through milk, water, or food, and chronic carriers have not been demonstrated. As the disease is transmitted by direct contact from person to person during the early stages the actual source of infection is not recognized until after the transmission of the disease has occurred. Authorities are agreed that measles is not transmissible during the period of incubation but that it is most contagious in the period of invasion or prodromal period. It is contagious in the stage of eruption. That it is not contagious during the periods of desquamation and convalescence is the generally accepted view. When measles occurs in a family all susceptible persons should be quarantined for at least two weeks after the last exposure. This means keeping the children strictly away from other children. It is not necessary to restrict the activities of members of the family who have had measles or to exclude from the house visitors who have had measles. A second attack is most uncommon. The mother and nurse should take every precaution not to carry the disease to others, although this is a very rare occurrence. To avoid the possibility, however, they should wear a gown

to avoid contamination of the clothes. The attending physician should scrub his hands with soap and water after coming in contact with a case of measles and refrain from coming in contact with susceptible children immediately after seeing a case of measles. No elaborate measures to disinfect the room, clothing or other articles at the end of isolation is necessary. The virus of measles rapidly loses its virulence and does not cling to objects. The sick room should be thoroughly scrubbed and then aired for twenty-four hours. A few hours of exposure to the air and sunlight with open windows will make it safe for occupancy.

Schools and Kindergartens.—When measles breaks out in a community the question of the schools in that locality immediately arises. Ruhräh believes that in order to protect the younger children the schools should be closed at the beginning of an epidemic in order to prevent the transmission of the disease by the older children who attend school to the younger ones at home. This meets with objections from school authorities on account of the loss of time involved.

The best method is to keep an accurate record of the illnesses of all pupils on file so as to know who are susceptible and who are immune. Parents should be notified when a case is reported and susceptible children excluded from school until fourteen days after the occurrence of the first case. Prompt action is necessary as soon as the first case develops, for only a few seconds' exposure will transmit the disease and it will spread with great rapidity and soon be beyond control. The exclusion of all susceptibles is a surer and safer method than the daily inspection of pupils for the first signs of measles. This would not mean closing the schools, as a very large proportion of the pupils will be found to have had the disease. It may be advisable and desirable in the presence of an epidemic to close the kindergarten or first grade.

Hospitals and Institutions.—When a case of measles breaks out in a hospital or institution all the children in the ward should be isolated and no new patients or children admitted, for at least eighteen or twenty-one days after the appearance of the last case. Absolute security cannot be assumed until three weeks have elapsed without the appearance of new cases.

Hospital epidemics are often attended with a high mortality and every means should be taken to prevent spread; rigid cleanliness and technic must be employed both by nurses and physicians.

When proper provision cannot be obtained in the home it is a wise plan to send the child to a hospital for contagious diseases if such is available.

Protective Inoculation.—The greatest advance in recent years in the prevention of measles has been in the production of immunity. The use of serum obtained from the blood of patients convalescing from measles has been used as a prophylactic agent for about ten years. Degwitz reported

a series of one thousand susceptible children who were inoculated and the results showed that 85 per cent of those injected did not develop measles. Von Torday reviewed two thousand cases in 1923 which had been injected and found that over 97 per cent escaped the disease. Recent literature contains many references on the favorable results obtained by such inoculation. For example, Toomey injected 389 patients in hospitals and children's institutions in Cleveland with from 3 to 10 c.c. of measles convalescent serum intramuscularly. Only twenty-one of these patients or 5 per cent contracted measles, thirteen before and eight after the usual incubation period of fourteen days, and the disease was very mild and attenuated in all of the injected cases. The method of taking blood from the donor is as follows: One week to ten days after the appearance of the eruption the blood is withdrawn from the median vein by inserting a 15 gauge Luer needle and allowing the blood to run directly into a 500 c.c. sterile bottle containing 20 c.c. of a 25 per cent solution of sodium citrate with a small quantity of tricresol as a preservative. The bottle should be shaken while the blood is being drawn off. The dose is 5 c.c. and it has been shown there are no advantages in larger doses. Park thinks it should be doubled for older children or when given late.

The blood of persons who have had the disease contains a certain amount of antibodies but not in the same amount as the convalescent case. When the serum is not available 20 or 30 c.c. of blood obtained from the parents can be injected directly into the buttocks of the young child and a temporary immunity can be obtained. Owing to the technical difficulties and the pain resulting from so large injections, this procedure is justifiable only in exceptional cases. The duration of this passive immunity is from three to six weeks. This shortness of protection limits the use of the serum to infants and delicate children who are not in fit physical condition to stand any illness.

A review of injected children who developed measles shows that under ordinary conditions it occurs in an extremely mild form in which many of the symptoms are absent and the temperature falls quickly. A favorable feature of this modified type of measles in injected children is that it seems to afford a permanent immunity, while those children who entirely escape after the injection are liable to contract measles during a later exposure.

It has been shown that the chances of preventing the disease are greater if the contact is not continued and the serum is injected not later than five days after the first exposure.

The injection of convalescent measles serum can be said to afford a temporary immunity against measles, but on account of the difficulty in obtaining the serum and the shortness of protection its use must be limited to very young children and to hospitals and children's institutions.

Active Immunization by Inoculation of the Virus of Measles.—Her-mann advocated active immunization of young infants by inoculation of the infectious material on the nasal mucous membranes. The method followed is to obtain the nasal mucous discharge of patients coming down with measles in the stage of invasion one to two days before the appearance of the eruption, and mix it with a small quantity of normal salt solution. This is then centrifuged to remove bacteria and other extraneous material and a little tricresol added as a preservative. A few drops of this are applied to the nasal mucous membranes of the infant to be immunized. Only healthy infants between four and five months of age are inoculated, as they are relatively immune if their mothers have had measles. A reaction consisting of a slight fever appears from the eighth to the sixteenth day and occasionally a few spots on the face and body. In all his inoculations he has not had any infant exhibit any unfavorable symptoms. He believes the immunity will last several years and tide the child over the dangerous period.

Ferry and Fisher prepared an antitoxin by injecting horses and rabbits with measles toxin obtained from the so-called *Streptococcus morbilli*. This antitoxin is concentrated and refined by the usual methods and they have been able to concentrate this measles antitoxin several times as high in neutralizing power as the measles convalescent serum.

Tunnicliff was able to develop an immune goat serum which has been very successfully employed as a prophylactic. Its great advantage lies in the question of supply, for it can be made available for use at any time and in greater quantities than is possible in respect to human convalescent serum. Tunnicliff and Hoyne after an exhaustive trial which included tests by well-known pediatricians in various parts of the country found that if inoculated within four days after exposure protection against infection was obtained in 97 per cent of the cases. The duration of this passive immunity is the same as with human serum, but it is valuable in preventing measles in young and delicate children and in stopping an epidemic in hospitals and institutions where the mortality may be high and the inconvenience and expense may be great.

Prevention of measles in young children can be accomplished with the hearty coöperation of parents, physicians and health officers. The public must be made to realize that measles in children under three years of age is a dangerous disease and that over 75 per cent of the deaths from measles occur in children of that age period. Godfrey advocates a card catalogue of all children under three years of age by the health officer, the object being to notify each family when an epidemic appears and emphasize the danger of measles to children under three years of age. The parents should be informed that the outbreak will last from two to six months, and during this period they should keep these young children to themselves as much

as possible and avoid all public gatherings and conveyances. They should play only with children known to have had measles. If one of the older children contracts the disease the baby should be at once isolated. When an older child is known to have been exposed the baby should be kept away from him for at least eighteen days. In the crowded tenement districts the problem is more difficult and here it is advisable for the health officer to try and have the young and delicate children who have been exposed given inoculations of immune serum.

General Treatment.—The management of a case of measles should be carried on so as to give comfort to the patient. Measles is a self-limited disease and as yet no specific treatment has been discovered. Symptoms, complications and emergencies must be treated as they arise.

There are so many deep-rooted superstitions in the management of measles that it is difficult to convince parents that the little patients should be treated with common sense and a consideration for the comfort of the child. A child with measles should be kept in bed until two days after the rash and fever have disappeared. The bed should be screened to protect the child from draft and bright sunlight. It is not necessary to have the room dark and the windows closed. The room should be ventilated with plenty of fresh air. The temperature of the room should not be over 70° F. and drafts and cold air are to be avoided. The child should not be bundled up in woolen sheets and an excess of coverings. There is no objection to bathing the child each day with lukewarm water, care being taken to avoid undue exposure. The nightgown should open up in front so as to permit an easy examination of the chest.

The itching and burning of the skin can be relieved by sponging with alcohol or a bicarbonate of soda solution. Talcum powder can be freely dusted over the skin. Inunction of carbolized vaselin or some mentholated ointment often gives relief.

The bowels should move each day and simple laxatives, such as citrate of magnesia, milk of magnesia, cascara, etc., may be used. It may be necessary to inject a suppository or give a low enema.

The diet should be light and plenty of fluid is desirable. Children show a distaste for food and it is very foolish to force food early in the disease. Water either plain or carbonated should be given freely and there is no objection to giving lemonade, orangeade, ginger ale, grape juice, etc. In the acute stage fluid is more indicated than food. Milk may be used in any form unless it causes vomiting or distention. Later on, eggs, broths, cereals, scraped beef and simple desserts can be given.

The eyes should be protected if there is any conjunctivitis. Iced cloths can be placed over the eyes and the eyes kept clean by the frequent use of

boric acid solution. If the conjunctivitis is severe a drop of a 10 per cent solution of argyrol or 1 per cent solution of mercurochrome should be instilled in the eyes three times a day. The simple ointment of white vaselin or 1 per cent yellow oxid of mercury should be applied to the lids. The eyes should be carefully watched for several days after the attack.

The care of the mouth is important. It should be cleansed after eating with some simple mouth wash of normal salt solution. If sprue appears the buccal mucous membrane should be painted with a 3 per cent solution of nitrate of silver. For ulcerative stomatitis a mouth wash of 2 per cent solution of chlorate of potash should be used and the gums painted with a weak solution of iodin.

The nose can be irrigated with a fairly normal hot salt solution or a simple antiseptic spray. After the irrigation a few drops of mineral oil or some oil spray should be applied to remove crusts and to keep the nares open. If the congestion is severe and it is difficult to breathe, relief can be obtained by the application of adrenalin. Steaming with benzoin or creosote soothes the irritation in laryngitis and trachitis. If stenosis appears diphtheria antitoxin should be administered in large doses without waiting for the results of a bacteriological examination. Antispasmodics such as antipyrin, sodium bromid, benzol benzoinate, etc., may be given.

The cough of measles is characteristic and due to pharyngeal irritation. For its relief small doses of paregoric or codein are indicated. It is not advisable to use cough syrups as they are apt to cause fermentation and upset the stomach. The use of barbituric acid derivations, known under the trade names of allonal, amytal, etc., gives prompt and effective relief for this type of cough.

Diarrhea is often a troublesome symptom and can be controlled by cutting down the food or limiting it to boiled milk, toast, rice, etc. Hot fomentations over the abdomen are indicated if there is pain or distention. A preliminary dose of castor oil followed by six hours of starvation is generally all that is necessary to relieve this condition. If there is much mucus with tenesmus, colon flushings with bicarbonate of soda will be helpful. It may be necessary to use bismuth and opium to overcome the frequent stools.

The temperature can be controlled by the use of cold packs and ice to the head. Antipyretic drugs should be avoided but small doses of aspirin and phenacetin are often of decided benefit.

Nervous symptoms which accompany severe infections are treated as they arise. Convulsions are held in check by luminal, chloral and bromid, and relief often results from a lumbar puncture. Convulsions are often associated with hyperpyrexia which should be controlled with cold com-

presses. This will relieve the delirium and mental excitement as well as the stupor and coma which accompany some of the severe cases. The use of cold compresses and ice applications does not increase the liability to pneumonia nor retard the appearance of the eruption.

Cold extremities, feeble pulse and cyanosis associated with high temperature should be treated with hot applications or mustard pack, although ice should be placed on the head.

Acute bronchitis is relieved with steam inhalations and simple expectorants such as ammonium chlorid or ipecac. In order to diminish the chances of pneumonia, patients should be kept in bed as long as there are any physical signs in the chest. The treatment of bronchopneumonia associated with measles is the same as in other conditions. When cases of pneumonia occur in a hospital or institution they should be separated from the uncomplicated cases. The microörganisms most frequently involved in pneumonia complicating measles are the pneumococcus, streptococcus hemolyticus, and the influenza bacillus. As these are found in the mouth and are communicable, it is a wise plan to insist on systematic disinfection of the nose and mouth.

PUBLIC HEALTH REGULATIONS

The Sanitary Code established by the Public Health Council of the State of New York contains several ordinances relating to measles: "It shall be the duty of every physician to report to the local health officer within whose jurisdiction such patient is, the full name, age and address of every person affected with measles within twenty-four hours from the time the case is first seen by him. Such report shall be by telephone or telegram when practicable, and shall also be made in writing."

Superintendents or persons in charge of hospitals, institutions or dispensaries are also required to report all cases of measles admitted occurring therein. School-teachers where no physician is in attendance must report to the principal all facts relating to the illness and physical condition of any child under their jurisdiction who appears to be affected with a disease presumably communicable, and the principal shall report the facts to the local health officer and send the child home. The same is required by the head of a household, proprietor or keeper of any hotel, boarding house, or lodging house as well as by visiting nurses and public health nurses and persons in charge of labor or other camps, and by the master of any ship lying within the jurisdiction of the state. This applies only when no physician is in attendance and applies to all communicable diseases.

When the physician diagnoses a case of measles he must "secure such isolation of the patient or take such other action as is required by the

special rules and regulations which from time to time may be issued by the local health authorities or by the State Department of Health."

It is not necessary to quarantine adults as "when a person affected with a communicable disease is properly isolated on the premises except in cases of smallpox, adult members of the family or household who do not come in contact with the patient or with his secretions or excretions, unless forbidden by the health officer, may continue their usual vocation, provided such vocations do not bring them into contact with children nor require that they shall handle food or food products intended for sale."

No patient with measles can be carried or removed from or to any hotel, boarding house, lodging house or any dwelling without the permission of the local health officer.

The physician or nurse or other necessary attendant upon a case of measles after attendance upon the case shall take precautions and practice measures of cleansing or disinfection of his person and garments to prevent the conveyance to others of infective material from the patient.

The code states in regard to exposure of persons affected with measles: "No person shall permit any child, minor or other person under his charge affected with measles to associate with others than his attendants. No person affected with measles shall expose himself in such manner as to cause or contribute to, promote or render liable their spread." It also prohibits "the visiting, association or contact of any child, minor or other person under his charge with any person affected with measles."

Provision is made for the exclusion from public, private and Sunday school, or any public or private gathering, of any child suffering from a communicable disease. "Such exclusion shall be for such time and under such conditions as may be prescribed by the local health authorities." This may be also applied to members or inmates of a household where a case of measles is present or has occurred within fifteen days. No child affected with measles or that has been exposed to measles within fifteen days is permitted to come in contact with or visit any child who has not had such disease or any child in attendance at school.

The maximum period of incubation of measles is placed at fourteen days. The minimum period of isolation for measles is stated as until at least five days after the appearance of the rash.

The attending physician should be familiar with these regulations so he can be in a position to advise the family and to conduct the case in accordance with requirements of the public health law.

The American Public Health Association adopted at its annual meeting in 1926 a set of standards for the control of communicable diseases. Those in regard to measles are as follows:

1. INFECTIOUS AGENT.—Unknown.

2. SOURCE OF INFECTION.—Buccal and nasal secretions of an infected individual.

3. MODE OF TRANSMISSION.—Directly from person to person; indirectly through articles freshly soiled with the buccal and nasal discharges of an infected individual. The most easily transmitted of all communicable diseases.

4. INCUBATION PERIOD.—About 10 days.

5. PERIOD OF COMMUNICABILITY.—During the period of catarrhal symptoms and until the cessation of abnormal mucous membrane secretions—minimum period of nine days; from four days before to five days after the appearance of the rash.

6. METHODS OF CONTROL

(a) The infected individual and his environment

1. *Recognition of the Disease.*—Clinical symptoms. Special attention to rise of temperature, Koplik spots and catarrhal symptoms in exposed individuals.

2. *Isolation.*—During period of communicability.

3. *Immunization.*—By the use of the serum or whole blood of convalescent measles patients, or of any healthy adults who have had measles, given within five days after exposure to a known case of measles, the attack in the exposed person may be averted in a high percentage of instances; if not averted, the disease is modified. Given later, but at a time prior to the clinical onset of the disease, convalescent serum usually modifies the severity of the attack and the patient acquires the usual lasting immunity to the disease.

4. *Quarantine.*—Exclusion of exposed susceptible school children and teachers from school until 14 days from last exposure. This applies to exposure in the household. Exclusion of exposed susceptible children from all public gatherings for the same period.

5. *Concurrent Disinfection.*—All articles soiled with the secretions of the nose and throat.

6. *Terminal Disinfection.*—Thorough cleaning.

(b) General measures

1. Daily examination of exposed children and of other possibly exposed persons. This examination should include record of the body temperature. A nonimmune exposed individual exhibiting a rise of temperature of 0.5° C. or more should be promptly isolated pending diagnosis.

2. Schools should not be closed or classes discontinued where daily observation of the children by a physician or nurse is provided for.

3. Education as to special danger of exposing young children to those exhibiting acute catarrhal symptoms of any kind.

4. In institutional outbreaks immunization with convalescent serum of all minor inmates who have not had measles is of value in checking the spread of infection and in reducing mortality.

CHAPTER IV

GERMAN MEASLES

Definition.—German measles is an acute, specific, communicable disease characterized by a short invasion with mild indefinite symptoms lasting but a few hours and followed by a characteristic eruption. The constitutional symptoms are mild and the disease is of short duration.

Synonyms.—Rubella, Rötheln, rubeola.

History.—The first detailed description of rubella is found in an article written by a German named Wagner in 1835, which no doubt explains its popular name. Wagner's belief that it constituted a distinct clinical entity was not accepted by the medical profession and there was much bitter controversy over this question. Many authors believed it to be a new and mild form of measles, some confused it with scarlet fever, while others considered it a hybrid of measles and of scarlet fever. The term rubella is found in earlier writers, but its identity was not established until 1881.

The question of its classification was fully discussed at the International Congress of Medicine which was held in London in 1881. The proof there presented by the most distinguished authorities of Europe and the United States removed any doubt of its existence as a separate and distinct disease.

Etiology.—German measles is communicable without any doubt, but less so than measles or scarlet fever. The character of the contagion is unknown; also similar methods and media which were used with some success by Tunnicliff in measles were without any result in this disease. It cannot be inoculated into monkeys as is the case in measles, and no one has succeeded in cultivating any organism from the blood.

The susceptibility is not high and it is estimated that only about 30 per cent of children exposed will contract the disease. This varies, however, in different epidemics. The absence of severe catarrhal symptoms with coughing and sneezing and the very short period of invasion may account for its slight contagiousness. Most observers claim that infection is more apt to take place in closed rooms than in the open air. This belief is strengthened by the fact that epidemics usually prevail in winter or spring when children are compelled to spend much of their time indoors. Reports of epidemics in orphan asylums and institutions where children are closely quartered show that it spreads quite rapidly. Ashley calls attention to a peculiarity of this disease, in that if an individual who resides in a community where German

measles is prevalent goes to another, while in the stage of incubation, and comes in contact with others he will suffer from an ordinary attack and no further cases will occur in the new locality. One attack usually confers immunity for life, although second attacks have been reported.

It can be stated positively as a fact that an attack of German measles does not protect from an attack of measles or scarlet fever, nor does an attack of measles or scarlet fever furnish any immunity from German measles. This is the consensus of opinion after fifty years of careful observation. There are instances where children, during a short period, have had measles, German measles and scarlet fever. When a case of German measles appears in a school or institution it will breed true.

Age.—As in other communicable diseases there seems to be a natural immunity against German measles in infants under six months of age. The age of greatest susceptibility is in children from four to ten years of age. This is a little later than that of measles. Adults of all ages may contract this disease and a case has been reported in a woman of seventy-three.

Mode of Infection.—This is a contact disease and is not carried by a third person or by articles of clothing or inanimate objects. The contact must be intimate. The contagion is probably contained in the discharges from the nose and throat and may be transmitted by coughing, talking or sneezing. The consensus of opinion is that it is contagious only in the stage of invasion and after the appearance of the eruption it cannot be spread.

Symptoms.—*Period of Incubation.*—This has been placed by different authors as ranging from ten to twenty-one days, while the average duration appears to be about fourteen days. The patients show no symptoms during this period. A prodromal rash lasting from a few hours to two or three days has been observed by some writers. No one has ever seen Koplik's spots either in the prodromal or eruptive stages of the disease.

Period of Invasion.—This is very short and in many cases is absent. The symptoms are a vague malaise, loss of appetite, slight discomfort in swallowing and very mild catarrhal symptoms. During this period the disease is undoubtedly communicable. The enlargement of the cervical and occipital lymph-nodes which is so characteristic of the disease first appears in this period and is accompanied by a slight rise in temperature. The lymph-nodes most frequently affected are the postcervical group. They may reach the size of a hazel nut and may be slightly tender to the touch. They are present on both sides of the neck and form a chain extending the length of the neck and are plainly visible when the patient turns his head to one side. The other lymph-nodes, namely, axillary, epitrochlear and inguinal, may also be involved but not with the same constancy as the

postcervical and occipital. They first appear before the eruption and may last several days after the disappearance of the rash. Klaatsch, in writing of the enlarged lymph-nodes, said: "This symptom is so constant that one could make a diagnosis in the dark by means of the sense of touch provided he knew there had been an acute infectious exanthem present."

There may be a slight rise in temperature a day before the appearance of the rash, but it is more often absent than present.

Period of Eruption.—In a majority of cases the first symptom is the rash. It is the eruption that first calls attention to the disease. This eruption appears first on the face, especially on the bridge of the nose and the upper lips and spreads downward very rapidly. It is seen as an enanthem on the mucous membrane of the mouth and palate, but it does not show the distinctive enanthem of measles but consists of very minute bright-red spots. On the extremities the eruption is generally on the flexor surfaces. The eruption may spread over the entire body and extremities within twenty-four hours. It fades first on the face after two or three days and then over the rest of the body, and the entire period of eruption does not last over three or four days. The color and character of the rash vary in the same and in different epidemics. It most commonly bears some resemblance to measles with discrete maculopapules and the term "rubella morbillosa" has been applied to these cases. Another group of cases shows a very fine pale-red punctate rash which may appear confluent over the face and looks like scarlet fever. These cases have been called "rubella scarlatinosa" and some question has been raised as to their proper classification.

There is no question but that the character of the eruption in rubella is subject to considerable variation. It is very seldom that one sees a patient with the entire eruption at the same time, as the rash may have faded on one part of the body and fully developed on another. The fading of the rash leaves behind it a very slight pale brownish discoloration. There may be a slight itching of the skin during the eruption. The eruption is usually not followed by desquamation, although it has been observed in some cases. It is usually very slight and discovered only on close examination, but it is sometimes found in large flakes. There is a little fever when the eruption appears, but this rarely rises over 102° F. and returns to normal after two or three days with morning remissions.

Complications.—These are rare and some of those reported may have been connected with other diseases. There may be some soreness of the joints but it is mild and only lasts for a few days. Cases of nephritis following German measles have been reported. Cardiac complications do not occur. Second attacks are very rare.

A rather unusual and atypical epidemic of German measles was studied by the writer in 1901. This occurred in a small village of about four

hundred inhabitants. Nearly one-half of the population contracted the disease. The majority of the patients were adults and out of 147 cases of which the local physician kept a record 81 or 60 per cent were in persons over twenty years of age. No child under twelve months developed the disease. In one family the father, mother and four children had the disease, while an eight months baby escaped. The period of incubation averaged nineteen days. One patient went to her home some miles distant and after a few days came down with the disease. Exactly twenty-one days later her sister came down with the same rash. The onset was sudden and in the more severe cases was attended by feelings of malaise, headache, sore-throat and slight fever. There was no sneezing, coughing or redness of the conjunctivæ in any of the cases.

Enlargement of the lymph glands was a constant manifestation of the disease in every instance. The chain of lymph-nodes situated along the posterior border of the sternocleidomastoid muscles were invariably palpable. In severe cases those of the groin and axilla were enlarged. They showed no tendency to suppurate or break down, although they could be felt in some cases for several weeks after the attack. The glands were enlarged even in the mildest cases where the only symptom was a faint rash. The pulse was not rapid and the highest temperature observed was 102.5° F. The urine was examined in over a hundred cases and in several in which desquamation had occurred, and in no instance was any albumin detected. No complications on the part of the kidneys were observed. The skin lesions on superficial examination looked like those of scarlet fever, as the color was bright red with a fine rash. Closer examination revealed a macular quality which was not wholly lost over areas where the eruption was apparently fully confluent. There was a greater intensity in spots with fading to a lighter hue between them. Over other areas the mottled appearance was pronounced, showing spaces of clear or but slightly congested skin. In some instances there was more dullness of color, an approach toward the tint of measles, and the contrast was appreciable between these types in members of the same family seen side by side. There was not the punctate redness so characteristic of scarlet fever. Its behavior on pressure was different from that in scarlet fever; instead of the prolonged blanching with red puncta of deeply congested papillæ which characterizes the scarlatinal rash, there was uniform but transient blanching on pressure.

The duration of the active skin lesion was about a week. The eruption was universal. The eruption was followed by a fine branlike desquamation but in a number of cases where the rash had been intense there was flaky desquamation of the hands and feet. In no case was there any desquamation of the tongue producing the characteristic strawberry tongue of scarlet

fever. Not a single death occurred and the benign quality of the epidemic was remarkable as so many persons were affected and some were severely ill.

The endemic character of this outbreak was very remarkable. No attempt was made to quarantine the individual patients or the village as a whole, yet only a few isolated cases appeared in the neighboring towns. There were several instances of persons who left the village during the epidemic and came down with the disease in distant parts, sometimes communicating it to their immediate associates, yet in no instance did it spread where thus transplanted.

Diagnosis.—This may be difficult in sporadic cases, and mistakes can easily be made as it so closely resembles mild measles in an abortive form or even mild cases of scarlet fever. A diagnosis can usually be made without difficulty during an epidemic.

Measles.—The absence of prodromal catarrhal symptoms, high fever in the stage of invasion, incessant hard dry cough and especially the absence of the Koplik spots on the buccal mucous membrane and on the gums would rule out a diagnosis of measles. In measles the lymph-nodes are not enlarged in chains as in rubella. These diseases breed true and an atypical case of measles would spread measles and no other disease to other susceptible children. The period of invasion is much longer in measles and the incubation is shorter. The urine in measles gives the diazo-reaction, while in German measles this is absent. In measles in the prodromal stage there is a lymphopenia, while in measles there is a lymphocytosis. A history of a previous attack of measles practically rules out a second one. This is often an aid in diagnosis if it can be confirmed, as very often in early childhood a rash from indigestion or anaphylaxis is often called measles.

Scarlet Fever.—Even though the eruption may at first glance look like scarlet fever no one is justified in making a diagnosis of any of the exanthemata on the appearance of the rash alone. The other symptoms are more characteristic. No one should confuse this disease with scarlet fever when it is found that there was no sudden onset with vomiting, sore-throat, strawberry tongue, rapid pulse and high fever. The chain of enlarged cervical lymph-nodes, small and not painful and easily rolled about under the fingers, is never present in scarlet fever. The rash in rubella very rarely desquamates in large flakes or as completely as in scarlet fever. Many complications follow scarlet fever, especially on the part of the kidneys and heart, and scarlet fever not infrequently ends fatally.

Antitoxin rashes, drug eruptions and reflex skin lesions from the intestinal tract may closely simulate the eruption of German measles. The history of the case and the absence of enlarged lymph-nodes and the course of the eruption would clear up the diagnosis.

Prognosis.—The course of this disease is invariably towards complete and uncomplicated recovery. There have been no authentic cases that have ended fatally from the effects of the disease.

Treatment.—*Prevention.*—The health department regulations classify German measles as a communicable disease and require it to be reported. Patients with this disease are excluded from school and public gatherings. Quarantine and isolation are not required, however, as it is less communicable and less dangerous than measles or scarlet fever. Isolation in the home is desirable in order to prevent its spread. The greatest detriment lies in the amount of time lost from school on account of the two weeks period of exclusion required by the health authorities. This disease is difficult to isolate as the patient does not feel ill or uncomfortable and the rash disappears in a few days. The long period of incubation and the short stage of invasion make it almost impossible to control. A physician is only called in a small proportion of the cases and then only to give advice because the parents fear it may be a case of scarlet fever or measles.

General Treatment.—In most cases none is required. Rest in bed during the appearance of the rash is desirable. A mouth wash and spraying the nose with a normal salt solution is of benefit when there are catarrhal symptoms. A light diet should be given when fever is present. The enlarged lymph-nodes require no treatment, as they are not painful and never suppurate. Individual symptoms can be treated as they arise.

Public Health Regulations.—German measles is a communicable disease and as such must be reported to the local health officer. In many places it is not strictly quarantined but children suffering from the disease are excluded from school until recovery and disinfection of person and at least seven days from onset. The New York State Department of Health provides that no person affected with German measles shall be permitted to come in contact with or to visit any child who has not had such disease or any child in attendance at school.

The Committee on Standard Regulations for the Control of Communicable Diseases of the American Public Health Association summarizes German measles as follows:

1. INFECTIOUS AGENT.—Unknown.

2. SOURCE OF INFECTION.—Secretions of the mouth and possibly of the nose.

3. MODE OF TRANSMISSION.—By direct contact with the patient or with articles freshly soiled with the discharges from the nose or throat of the patient.

4. INCUBATION PERIOD.—From fourteen to twenty-one days.

5. PERIOD OF COMMUNICABILITY.—Eight days from onset of the disease.

6. METHODS OF CONTROL

    (*a*) The infected individual and his environment

1. *Recognition of the Disease.*—Clinical symptoms.
2. *Isolation.*—Separation of the patient from nonimmune children, and exclusion of the patient from school and public places for the period of presumed infectivity.
3. *Immunization.*—None.
4. *Quarantine.*—None.
5. *Concurrent Disinfection.*—Discharges from the nose and throat of the patient and articles soiled by discharges.
6. *Terminal Disinfection.*—Airing and cleaning.

(*b*) General measures—None.

NOTE—The reason for attempting to control this disease is that it may be confused with scarlet fever during its early stages; each person having symptoms of the disease should therefore be placed under the care of a physician and the case should be reported to the local department of health.

CHAPTER V

CHICKENPOX

Chickenpox is one of the acute exanthematous diseases common to children. It is highly contagious. It is characterized by an eruption first macular and rapidly becoming vesicular. These tend to occur in crops and dry in a few days leaving a crust or scab. There is usually a slight fever which begins with the first appearance of the rash. One attack generally affords immunity for life, and serious or severe complications are very rare.

Synonyms.—Varicella, variola notha, variola spuria; Varicellen, Windblattern, Wasserpocken, Schafpocken; la varicelle, la vérolette; ravaglione, morviglione.

HISTORY

The chief interest in the history of this disease lies in the controversy concerning its identity and relationship with smallpox. Most of the early writers were convinced that varicella was a mild form of variola and that both had a common origin. Hebra believed them to be the same disease and classified them according to severity. All cases terminating in three weeks were varicella, four weeks or over were variola.

It would seem from available data of medieval medicine that Vidus Vidius in 1626 recognized the clinical picture of chickenpox and differentiated it from smallpox. Vidius named the disease crystalli. Heberden wrote an excellent description of chickenpox in 1767 in which he said: "The chickenpox comes on without much fever. In the beginning the eruption resembles the true smallpox but the pustules increase faster and sooner go off. They likewise vary considerably in size and are seldom very numerous. On the first day they are red; on the second day they have watery heads; on the third day they become yellow or often being broken, they subside; on the fourth or day following they are covered with a thin scab." He further states: "The crust covers the pocks on the fifth day, at which time those of the smallpox are not at the height of their suppuration."

It was not until the introduction of vaccination that chickenpox became generally recognized and its identity established.

Notwithstanding all this clinical proof a rather bitter controversy appeared in the medical literature which did not abate until after 1870 when

there was a widespread epidemic of smallpox in Germany. This afforded an excellent opportunity to settle the dispute. It was proved at this time (1) that inoculation with varicella produced only varicella; (2) that varicella cannot produce variola and vice versa, and (3) that varicella does not protect against variola and variola does not protect against varicella.

ETIOLOGY

The specific organism causing this disease has not yet been demonstrated. Several Italian investigators believe it is a filtrable anaërobic organism. Direct experimental inoculation from the clear and opaque fluids in the vesicles has given unsatisfactory and unreliable results. This is in direct contradistinction to smallpox which is very readily inoculated. The inoculation of one has never succeeded in causing the other. It is a well established fact that vaccination against smallpox is practically always successful, but it affords no protection whatever against chickenpox.

The infective organism is short-lived and apparently remains active for only a short time on clothing and other articles. Direct exposure seems to be necessary and it is doubtful if it is carried by a third person or through the air. The contagion probably enters the body through the upper air passages. It is extremely contagious, especially in young children, but it can readily be controlled by isolation. The duration of the infective period is not definitely known, nor has it definitely been determined if the infection exists in the scabs as in smallpox. For this reason it is wise to isolate the patient until the skin is free of the scabs.

Age.—This is essentially a disease of childhood. It does occur, but not frequently, in adults. This may be on account of the great majority of adults having had the disease in their youth. Cases in very young infants have been reported, but as a rule it is rare under six months of age.

Season.—While chickenpox is seen at all seasons of the year, yet it is more prevalent in the fall on account of attendance at school. In the large cities it exists sporadically throughout the whole year, but epidemics occur at frequent and irregular intervals.

Race.—Susceptibility of certain races has not been observed. Both the Negro, Mongolian and Caucasian races take the disease with equal facility.

PATHOLOGY

Unna excised one of the vesicles on the second day of its appearance and found that it was tent-shaped with the central point at the summit. The pathology of the vesicle differed in several points from one he studied from a case of smallpox. Studies of the lesion in different stages show the inflam-

matory processes are of the same nature, differing only in intensity and duration. The lateral walls rise from a broad base towards the apex and are divided by cellular partitions. The fluid is confined in these cellular partitions. These partitions or septa join in the covering or roof and not in the center of the base as in smallpox. Moreover, the septa are not as strong as those in the vesicles of smallpox. If the fluid is thrown out in large amount the septa are either absorbed by pressure or disappear from rupture. This explains why some of the vesicles appear unilocular and others multilocular.

The fluid of the vesicles is at first clear. It contains fibrin and coagulates when removed. It contains a few epithelial cells. It becomes turbid if infected by bacteria.

The cutis shows a marked dilation of the blood-vessels with a considerable enlargement and multilocation of the cells about the vessels. The base of the vesicle is concave and extends down to the level of the papillæ which are somewhat swollen and project slightly into the cavity.

The active destructive process is quickly followed by repair, and the absence of scarring or pitting is due to the superficial position of the vesicle, the absence of suppuration and the rapid repair of the lesion. If the fluid becomes infected or if the lesion is deep enough to involve the papillæ and the true skin, cicatrices will result. The more the infection the greater is the scar.

Blood.—There have been a few studies on the blood and this shows nothing characteristic. There is a slight leukocytosis with a slight increase in the number of eosinophils.

SYMPTOMS

Period of Incubation.—Different observers have assigned widely variant limits to this period. Schamberg regards fourteen to seventeen days as the usual period, although he has seen cases in which three weeks passed after exposure before the rash appeared. It is safe to state the limits from ten to twenty-one days. Schamberg relates the case of a physician's daughter who was isolated in a room in the upper story of her home on account of fever and sore-throat with an exudate. The next day the characteristic rash of chickenpox appeared. Her eight-year-old brother played with her the day before she was isolated and two days before the appearance of chickenpox. Sixteen days after playing with his sister who had been strictly isolated and quarantined he came down with chickenpox. This not only gave an accurate period of incubation but proved very conclusively that chickenpox is contagious at least two days before the clinical symptoms of the disease appear. This is analogous to the other exanthemata.

Period of Invasion.—In the vast majority of cases of chickenpox the eruption is the first sign of the disease and the rash is not preceded by a prodromal illness. Mothers usually state that the first symptom to attract their attention was the rash.

There may be some mild constitutional symptoms, such as malaise and a slight temperature. These may vary in duration from a few hours to two or three days. The child may appear restless and slightly feverish the night before the rash appears. Adults, on the other hand, are very apt to have a well-defined series of prodromal symptoms, such as chilliness, fever, nausea, loss of appetite, backache, etc. These symptoms may precede the appearance of the eruption by two or three days.

Several observers have reported a prodromal erythema which resembled scarlet fever, but this is exceedingly rare.

Period of Eruption.—The eruption is usually the first symptom. There is nearly always a slight rise in temperature with the appearance of the rash. It may be trifling and of short duration or in the more severe cases it may last for several days and rise as high as 104° F. The child's general condition is so little disturbed that it is difficult to keep the patient in bed. The nights may be restless and there may be a loss of appetite and a feeling of general indisposition.

The eruption first appears on the face and back as small macules and papules; in a few hours it is seen all over and in all parts of the body. The macules either remain small and disappear or enlarge and form papules about the size of a pea. These develop into vesicles in a short time. A characteristic feature is that all stages of the eruption—macule, papule and vesicle—may be seen at the same time on the patient. Huebner likens the appearance of the back to an astronomical map where irregular stars of various sizes are situated close together. After a few days the fluid contents of the vesicles are absorbed and a yellowish brown scab remains. This usually falls off in a few days without leaving any scar. As a rule the eruption causes very slight inconvenience, but sometimes it causes great discomfort and is accompanied with itching.

The location of the rash is characteristic. It is most frequent on the trunk and only occasionally in the palms of the hands or soles of the feet as in smallpox. It is found very frequently in the mouth, on the tonsils, gums, pharynx and hard palate. It is not at all uncommon in the scalp and on the mucous membranes, not only of the mouth but about the genitals. In the mouth they look like small canker ulcers or aphthous stomatitis. They seem to give very little pain as the children seldom complain on chewing and swallowing. The eruption in the mouth or exanthem does not develop into vesicles as it seems to develop more quickly in the mouth than in the skin. The vesicles may appear on the eyelid or on either the ocular or

palpebral conjunctiva. Cases are on record where the cornea was involved. These eye involvements cause much pain and suffering and may leave a corneal clouding.

The eruption is found more frequently on the genitalia of girls. It is rare to have any trouble with boys, but vulvitis and painful urination are not infrequent in girls. There is also the danger of infection through scratching or uncleanliness. This results in ulcers, necrosis, lymphadenitis or even a general septicemia. Cases have been reported where the eruption appeared in the larynx and trachea. Symptoms developed similar to croup— hoarse and stridulent coughs, cyanosis and dyspnea. Several of the reported cases resulted fatally. There have been no cases reported in which the chickenpox eruption appeared on the mucous membrane of the stomach or intestines. The eruption may all come out in one day, but as a rule it appears in crops on different days. There may be a distinct pause after which a new crop of vesicles appears. The eruption may be especially profuse under bandages, about the genital region. The pressure of the clothing, garters, etc., causes an irritation which results in a thicker crop of vesicles. This local irritation may cause the disease to run a much longer and more severe course than otherwise would be the case. One case is on record where the parents gave the child a mustard bath in the prodromal stage. When the eruption appeared it was very severe and there were over five hundred vesicles which became confluent and suppurated. Such extensive confluent eruptions are not frequent, although in nearly every case a few vesicles become confluent.

The number of vesicles is very variable. There are cases seen during epidemics in which only one or more vesicles can be found. On the other hand there may be as many as six or seven hundred.

The size of the vesicles varies greatly. They range from that of a pinhead to a surface as large as a silver dollar. When these vesicles become infected with pyogenic bacteria from scratching, constitutional disturbance, or when the disease is protracted, there may be destruction of the skin with permanent scarring. It is difficult or impossible to tell these scars from those the result of smallpox. The number of these scars, however, is not great and they have a tendency to decrease in size as the child grows older.

The duration of the disease after the first appearance of the eruption until the scabs fall off varies from five to fourteen days. The duration of the individual lesions of chickenpox is brief and only three days elapse as a rule from the time the vesicle appears until it dries up and forms a crust. If, however, the vesicle becomes infected with pyogenic bacteria the lesion may take a long time to heal and may even lead to a gangrenous ulcer.

Second attacks have been reported, but most of them have occurred within three weeks after the first attack and should be considered a relapse,

not a second attack. In an epidemic of chickenpox occurring in St. Margaret's Hospital for Babies where sixty-one babies had the disease, four of them came down with a well-marked eruption quite as intense as the primary rash within two weeks after the baby had apparently recovered. There is no reliable record of a case developing after a year from the first attack in which there could be no doubt as to the diagnosis in both attacks. It would seem, therefore, to be an established fact that one attack of chickenpox affords immunity for life.

COMPLICATIONS AND SEQUELÆ

On account of the mildness of this disease and the benign course it usually follows many authors pay slight attention to any possible dangers. Nevertheless, complications may and do occur which are sometimes fatal. The vesicles if ruptured may become the point of entrance for pyogenic and pathogenic organisms. Most of the complications arise from such infection.

A number of cases of nephritis developing in the course of chickenpox have been reported. While this is a rare complication yet it is a serious one and its possibility should be borne in mind. This generally appears in the first two weeks of the disease. While it is seldom severe, yet several cases of fatal nephritis have been reported. Acute hemorrhagic nephritis has been observed. Nephritis is usually mild and not associated with marked constitutional symptoms or change in kidney function. The urine contains casts. The presence of albumin without casts is much more frequent than in nephritis. Cerf classified the kidney involvement in chickenpox as follows: (1) Latent nephritis in which there are no symptoms, and albuminuria is only discovered when looked for; (2) light nephritis in which there is marked albuminuria and some edema but no severe symptoms, and (3) severe nephritis with fever, marked albuminuria, anuria, cramps, uremia, gastro-intestinal symptoms, etc. The occurrence of nephritis varies in different epidemics. It develops after the vesicles have dried up, and a severe attack may follow a light attack of chickenpox.

Secondary infections with the vesicle as the point of entrance of pus-forming bacteria are among the more frequent complications of this disease. These occur most often among children in poor sanitary surroundings; but the disease is no respecter of persons. Scratching and uncleanliness are the commonest causes. They are seen in the regions soiled by urine and feces in uncleanly children. The lesions are pustular and may resemble impetigo. Boils, abscesses and erysipelas may result from this infection. The neighboring lymph glands may become involved and enlarged and even undergo suppuration. A general pyemia may result with a fatal termina-

tion. A number of cases of thrombosis with severe general symptoms have been reported.

There is a serious complication, the result of infection, known as varicella gangrenosa. This is most frequent in weak, debilitated infants. The vesicle becomes enlarged and an ulcer develops which may become as large as a saucer. There are severe general symptoms with high fever; the patient rapidly sinks and a fatal termination is the rule.

Arthritis may occur during the eruptive fever or later. It usually affects several joints, but only one joint may be affected. From the cases reported of this complication there may be a simple synovitis or a severe suppurative form. The suppurative form may be the result of pyemia or extension of infection through the lymphatics from a neighboring site of infection. The prognosis of the synovitis form is good, but the suppurative cases usually terminate fatally.

The nervous system is less apt to be involved than in any of the other infectious diseases. Cases of chorea, paraplegia, multiple sclerosis and encephalitis have been reported as following chickenpox.

Bronchitis and bronchopneumonia have been reported as complications of chickenpox, but they are rare and their association with this disease may have been accidental.

Occurrence with Other Infectious Diseases.—This not infrequently happens. The diseases most commonly involved are measles, scarlet fever, diphtheria and smallpox. These may develop in children suffering from chickenpox, or the attack of chickenpox may occur during the convalescence of any of these diseases. Such double infections are not rare, as none of the communicable diseases of children afford immunity to each other in the same manner as cowpox does to smallpox. The writer has observed measles and chickenpox occur in the same patient at the same time.

Cases have been reported where an attack of chickenpox has followed one of smallpox. Schamberg reported an outbreak of chickenpox among thirty-three children convalescent from smallpox. Smallpox and chicken-pox may actually exist at the same time, which adds somewhat to the diffi-culties of diagnosis in severe cases. The writer attempted to vaccinate several children suffering from chickenpox, using a vesicle as a point of entry for the virus, but in no case did a positive vaccination result.

DIAGNOSIS

In the vast majority of cases there is no difficulty in making a diagnosis. There are a number of skin disorders that may be confusing on first examination, but watching the course of the disease for a few days will usually clear up the diagnosis. Among these skin diseases may be men-

tioned impetigo, pemphigus, drug eruptions, furunculosis, urticaria, heat
dermatitis, acne, etc. Pemphigus of the newborn has been confused with
chickenpox, but the longer duration of the pemphigus eruption and the
occurrence of chickenpox in other members of the family bear on the
diagnosis.

If chickenpox is not seen in the first stages and the vesicles are infected
it presents many similarities to impetigo contagiosa. In the latter disease
the mucous membranes are not involved nor do the lesions appear simul-
taneously in all parts of the body in impetigo. There are no constitutional
symptoms; the pustules spread from one spot to another and are generally
seen on the face. Chickenpox runs a much shorter course and the lesions
disappear without local treatment. The appearance of chickenpox in other
members of the family or the development of later ones in contact cases two
weeks after exposure are important points in arriving at a diagnosis in
difficult cases.

The chief diagnostic difficulty is to differentiate it from smallpox. For
purposes of comparison the differences between smallpox and chickenpox
may be summarized as follows:

Chickenpox	*Smallpox*
Incubation fourteen to twenty-one days.	Incubation ten to twenty days.
Affects any age but chiefly young children.	Occurs mostly in adults.
Practically no period of invasion.	Definite period of invasion of three days' duration.
Very slight or no constitutional symptoms, except in rare cases.	Fever and constitutional symptoms usually severe and characteristic.
Eruption appears on all parts of the body but is most profuse over covered surfaces.	Eruption most profuse over face and hands and over exposed surfaces.
Eruption commences as macules which may become vesicular within a few hours. The lesions vary in size.	Eruption begins as firm shotlike papules which slowly evolve into vesicles and then pustules. The lesions are uniform in size.
No secondary rise in temperature.	Secondary rise in temperature with the appearance of pustules.
Lesions are superficial and the base is not infiltrated.	Lesions are deep-seated and the base is infiltrated.
Vesicles are unilocular and collapse readily and do not become umbilicated.	Vesicles are generally multilocular and do not collapse and are often umbilicated.
Eruption comes out in crops on alternate or successive days and the lesions may be seen in all stages of development at the same time.	Eruption comes out without interruption in twenty-four or forty-eight hours. Lesions show a uniform development.

Chickenpox	*Smallpox*
Lesions usually last from two to four days terminating in soft, friable crusts.	Lesions last from ten to twelve days terminating in dense, firm crusts.
Disease is not influenced by smallpox or vaccination.	Vaccination affords immunity. Is not influenced by chickenpox.

Tyzzer believes a positive differential diagnosis can be made from a study of the contents of the vesicles. In chickenpox the vesicles contain large multinucleated cells which are not present in smallpox.

In a doubtful case the inoculation of the contents of the vesicle in the cornea of a rabbit will determine whether it is smallpox or chickenpox or other skin disorders. If the case is one of smallpox the characteristic reaction will take place within twenty-four hours and the test is negative to the contents of vesicles from other diseases.

Of course in every doubtful or suspicious case the child should be at once vaccinated.

PROGNOSIS

This is one of the mildest of acute infectious diseases of children, and while children occasionally die from the complications, none do from the disease itself. The septic cases are serious, but the gangrenous cases are dangerous and are usually fatal. A general impairment of health and lowering of resistance may result from chickenpox and this may predispose to tuberculosis.

TREATMENT

Prophylaxis.—There is no object in strictly quarantining a child with chickenpox unless there are other children in the household, institution or vicinity who are weak, undernourished or suffering from some other disease. It is a wise plan to allow healthy, vigorous children to take it. Those who arrive at adult age without ever having chickenpox are apt to contract it at inappropriate times and under embarrassing conditions.

Several investigators have claimed excellent results from prophylactic inoculations and vaccinations. These are only justifiable in exceptional circumstances or in children's hospitals and institutions. These procedures must be done during the earliest part of the incubation period in order to be effective. Hess has found that immunity to chickenpox can be obtained by intravenous injection of the contents of the vesicles.

General Treatment.—The child should be kept in bed during the eruptive stage and as long as there is any fever. In the great majority of cases no treatment is necessary. As soon as the vesicles dry and an examination of the urine shows that the kidneys are not involved, the child can leave the sick room. The temperature is usually so slight that no medication is

indicated. Cold compresses to the head and sponging the body with cool water is all that is necessary.

The itching which may be annoying may be allayed by lukewarm baths followed by a liberal dusting of some simple unscented powder. Sponging with a solution of bicarbonate of soda, 1 dram to a pint, is often effective. Relief can be obtained by rubbing each lesion with a small portion of carbolized vaselin. If the itching is severe it may be necessary to use small doses of antipyrin, phenacetin, allonal or amytal.

It is essential that the finger nails be closely trimmed and that the hands be kept clean. Some form of restraint, such as Hand-I-Hold mits or keeping the arms stiff with splints, etc., should be used with infants and very young children to prevent scratching.

Lesions in the mouth and ulcers in the throat should be subjected to antiseptic mouth washes, such as boric acid solutions, lavoris, glycothymolin, etc. The teeth should be cleansed with a soft cloth, and the use of the toothbrush should be prohibited. It may be necessary to touch the ulcers with a nitrate of silver pencil or a 2 per cent solution of mercurochrome.

Special care must be taken in washing the genital region, and powder should be applied to the parts, or if there is any inflammation some soothing ointment, such as cold cream, zinc oxid or boric acid, should be used.

Daily baths may be given in the mild cases, but care must be taken not to rub or irritate the skin, and very hot water should not be used. The skin can be dried by gentle patting.

Abscesses, enlarged glands and infections of the skin are treated according to the generally accepted surgical principles.

A simple diet avoiding rich and too sweet foods should be given, and care taken to insure a daily movement of the bowels. If the child does not pick up and recover his strength he should be carefully examined to determine, if possible, the underlying cause. A change of climate or special treatment may be advisable.

PUBLIC HEALTH REGULATIONS

The Sanitary Code of the New York State Department of Health includes chickenpox among the diseases that must be reported to the local and state health officials and forbids any person sick with the disease to attend any public, private or Sunday school, or any public or private gathering of children, "for such time and under such conditions as may be prescribed by the local health authorities, not inconsistent with the provisions of this code or the special rules and regulations of the State Department of Health." This also applies to children who live in a house where there is or has been a case of chickenpox within fifteen days. It does not, however,

apply to adult members of the family who do not come in contact with the patient or with their excretions and secretions, unless their business vocations bring them in close contact with children and require that they handle food or food products intended for sale.

Without permission of the health officer no child with chickenpox can be taken to or removed from any hotel, boarding house, lodging house or other dwelling or removed from any vessel to the shore.

The health authorities place twenty-one days as the maximum period of incubation, and the minimum period of isolation is designated "until twelve days after the appearance of the eruption and until the crusts have fallen and the scars are completely healed."

A child suffering from chickenpox should not return to school until all scabs have fallen off and not until at least twelve days from the onset. If the patient remains isolated at home other children in the household are excluded until termination of quarantine if they have not had the disease. If they have had the disease they can continue at school.

Chickenpox is summarized by the Committee on Standard Regulations for the Control of Communicable Diseases of the American Public Health Association as follows:

1. INFECTIOUS AGENT.—Unknown.

2. SOURCE OF INFECTION.—The infectious agent is presumably present in the lesions of the skin and of the mucous membranes; the latter appearing early and rupturing as soon as they appear, render the disease communicable early, that is, before the exanthem is in evidence.

3. MODE OF TRANSMISSION.—Directly from person to person; indirectly through articles freshly soiled by discharges from an infected individual.

4. INCUBATION PERIOD.—Two to three weeks.

5. PERIOD OF COMMUNICABILITY.—Until the primary scabs have disappeared from the mucous membranes and the skin.

6. METHODS OF CONTROL

    (*a*) The infected individual and his environment

        1. *Recognition of the Disease.*—Clinical symptoms. The chief public health importance of this disease is that cases thought to be chickenpox in persons over 15 years of age, or at any age during an epidemic of smallpox, are to be investigated to eliminate the possibility of their being smallpox.

        2. *Isolation.*—Exclusion of patient from school, and prevention of contact with nonimmune persons.

        3. *Immunization.*—None.

        4. *Quarantine.*—None.

        5. *Concurrent disinfection* of articles soiled by discharges from lesions.

        6. *Terminal Disinfection.*—Thorough cleaning.

    (*b*) General measures—None.

CHAPTER VI

SMALLPOX

Definition.—Smallpox is an acute and highly communicable disease ushered in by an acute onset with fever which lasts from two to four days when the eruption appears on the face, trunk and extremities, which passes through distinct stages of papule, vesicle and pustule with the formation of a scab, which, when it drops off, leaves a distinctive scar.

Synonyms.—Variola; la variole; Pocken, Blattern; vajuolo; viruelas.

HISTORY

This is one of the oldest diseases of which we have record. It is stated to have existed in China over a thousand years before the Christian era. Records are said to have been discovered in India showing that this disease had existed from time immemorial. Hippocrates, who lived about four hundred years before Christ, described vesicular and pustular eruptions which are believed to relate to smallpox. There can be little doubt but that it was a great scourge in the first century.

The term variola was first mentioned by Bishop Marius of Lausanne in a description of an extensive epidemic of smallpox that swept through France and Italy in the latter part of the sixth century. The early writers confused smallpox and measles. An Arab physician, Rhazes, who lived in Bagdad about A.D. 900, wrote a "Treatise on the Small-Pox and Measles" which contained perhaps the first accurate description of smallpox. He states that the "eruption of Small-Pox is preceded by a continued fever, pain in the back, itching in the nose and terrors in sleep." He must have recognized distinct differences between the two diseases when he writes "except that there is not in the measles so much pain of the back as in the Small-Pox; nor in the Small-Pox so much anxiety and nausea as in the Measles."

Metlinger who wrote perhaps the first book for physicians on the diseases of children in Germany in 1473 gave an excellent description of smallpox in children but classified measles or eruptions with the smallpox. The term smallpox was first used in order to distinguish the disease from syphilis which was popularly called pox or large pox.

The disease appeared as a plague in England about the tenth century when devastating epidemics occurred where "many died of small pokkes

both men, women and children." Hirsch states that smallpox was introduced into the West Indies shortly after the discovery of America. An epidemic occurred in Boston in 1649. Lord Macaulay in describing the ravages of smallpox in England in the seventeenth century wrote "that disease over which science has achieved a succession of glorious and beneficent victories, was then the most terrible of all ministers of death. The smallpox was always present filling the church yards with corpses, tormenting with constant fears all whom it had not yet stricken, leaving on those whose lives it spared the hideous traces of its power, turning the babe into a changeling at which the mother shuddered, and making the eyes and cheeks of a betrothed maiden objects of horror to the lover."

The practice of inoculation may have been extensively used in China over a thousand years ago, for ancient writers describe "sowing the smallpox" by introducing the scabs from a sick person into the nostrils of healthy individuals. The first authentic description of its use comes from the pen of Lady Mary Montagu, wife of the British Ambassador to Turkey. It was in general use in Turkey in 1674. Zabdial Boylston of Boston was the first to perform inoculation in this country in 1721 which was about the time it was introduced in England. Lady Montagu had her children inoculated and this procedure was rather extensively practiced in England up to the discovery of vaccination. An extract from one of Lady Montagu's letters describes the technic as well as the modified attack of smallpox:

. . . Apropos of distempers, I am going to tell you a thing that will make you wish yourself here. The smallpox, so fatal and so general amongst us, is here entirely harmless by the invention of engrafting, which is the term they give it. There is a set of old women who make it their business to perform the operation, every autumn in the month of September, when the great heat is abated. People send to each other to know if any of their family has a mind to have the smallpox; they make parties for this purpose, and when they are met (commonly fifteen or sixteen together) the old woman comes in with a nutshell of the best sort of smallpox and asks what vein you please to have opened. She immediately rips open that you offer to her with a large needle (which gives no more pain than a common scratch) and puts into the vein as much matter as can lie upon the head of her needle, and after that binds up the little wound with a hollow bit of shell, and in this manner opens four or five veins. . . . The children or young patients play together all the rest of the day and are in perfect health to the eighth. Then the fever begins to seize them and they keep their beds two days, very seldom three. They have very rarely above twenty or thirty on their faces (sic) which never mark, and in eight days' time they are all well as before their illness. Where they are wounded there remain running sores during the distemper, which I do not doubt is a great relief to it. Every year thousands undergo this operation, and the French Ambassador says, pleasantly, that they take the smallpox here by way of diversion, as they take the waters in other countries. There is no example of anyone that has died

from it, and you may well believe that I am satisfied of the safety of this experiment, since I intend to try it on my dear little son. . . .

Smallpox was a great disease scourge the world over before the introduction of vaccination. To-day it has been so entirely eliminated that we can scarcely realize the havoc it wrought in the human race. It was so prevalent that every one was expected to have it some time or other. The mortality in England during the eighteenth century as revealed in the "Bills of Mortality" shows that smallpox caused about one-twelfth of all deaths. It also revealed the almost unbelievable fact that of all the deaths in children under five years of age one-half were the result of smallpox. There was an historic epidemic of smallpox in Boston in 1752. The population was 15,684, of which number 5,998 had previously had smallpox. Nearly two thousand people fled from the city to avoid infection. During the epidemic 5,545 contracted the disease, while 2,124 were inoculated with it. The population at the end of the epidemic consisted almost entirely of persons who had survived an attack of smallpox.

FIG. 1.—SMALLPOX.
Skin lesions are most numerous on the face and hands and are fewest on the trunk.

PATHOLOGY

The skin lesions may cover the entire body or there may be only a few isolated spots. They usually appear on the skin and also on the mucous membrane of the mouth, pharynx and larynx. They are most numerous on the face and hands and are fewest on the trunk. The specific lesion is a focal degeneration of the stratified epithelium of the skin accompanied by serous exudation which, when fully developed, forms a characteristic multilocular pustule or pock. The skin lesion at first is a degeneration of the cells in the lower layers of the epidermis which is accom-

panied with a serous exudation which is contained in a reticulum formed by the degenerated cells. As the exudate increases the spaces of reticulum enlarge until the fibers rupture and form one cavity as the exudate becomes purulent. Recovery begins when this purulent exudate is absorbed and the lesion dries up and there is regeneration of the epidermis. This takes about two weeks. These lesions on the skin may be accompanied by hemorrhage, edema and cellular infiltration. The lesions on the mucous membranes differ in that the degenerative epithelial cells are cast off, as there is no horny restraining layer and the vesicle within the epidermis is rarely seen and it never develops into a pustule.

Many variations from the usual type are seen and there are several rather distinct types of the disease, from the abortive and mild form known as varioloid to the most severe hemorrhagic forms. The lesions of these various types show differences according to the character and extent of the eruption.

Mononuclear basophilic cells are found in the blood-forming organs such as the bone marrow, lymph-nodes and spleen. These become phagocytic and pass into the blood stream. They cause cellular infiltration in the testicles, kidneys, adrenals and liver. In the testicles they may produce a focal necrosis from pressure and thrombosis. The toxins produce focal degeneration in the blood-forming organs and may become diffuse in the liver, kidneys and testicles. This degeneration is due to toxins, not bacteria. Bacterial infection of the skin lesions occurs in nearly all of the severe cases, and the action of their toxins is probably responsible for acute degeneration of the liver and kidneys seen in severe cases. These bacterial infections are responsible for the complications of boils, cellulitis, etc.

ETIOLOGY

The organism which is responsible for smallpox is not definitely known, but it is now thought to be due to certain bodies found in the pustules known as the *Cytorrhyctes variolæ*. Renault in 1881 thought they were parasites. Guarnieri described them in 1892 as parasitic protozoa. They were found after experimental inoculation in the cornea of affected rabbits. Councilman and his associates in this country have confirmed the views of Guarnieri. Their presence is of diagnostic importance to differentiate between variola and vaccinia.

Other investigators believe that these bodies are not protozoa but are products of specific action of the diseased cells which surround the causative organism.

A number of bacteria, such as *Staphylococcus albus* and *aureus* and the *Streptococcus pyogenes*, are found in the pustules.

Age.—This is a disease to which young infants are very susceptible. Numerous instances of fetal infection have been reported. The earliest on record was of a fetus after four and a half months of pregnancy. The writer had a case in an infant three weeks of age whose birth occurred in a hospital where a case of smallpox had erroneously been diagnosed as chickenpox. After its discovery the mother with other patients was vaccinated, but the baby was not. She had a moderately severe attack and recovered. The susceptibility does not diminish with age, and exposed and unvaccinated adults will contract the disease. A case of a man eighty-nine years of age has been reported.

Individual and Race Immunity.—There are apparently some individuals who seem to be naturally immune to smallpox as is the case in other infectious diseases, but this number is probably small. A person who escapes one exposure may contract the disease at another time. One attack affords immunity for life. Cases of second attacks are exceedingly rare and reported instances may have been due to mistakes in diagnosis. Smallpox may coexist with other infectious diseases. There is a prevalent impression that the negro race is more susceptible, but this may be explained by the fact that this race is not so generally protected by vaccination as the white race.

Seasonal.—In this country most of the cases occur during the winter months, while in England the disease prevails equally in all seasons. It is said that in tropical countries the worst cases occur during the hot weather.

The morbidity rates in New York State from 1915 to 1925 inclusive as shown in Table X show no seasonal incidence of cases. There appears to be a marked increase in the number of cases every two or three years but they are just as frequent in the winter months as in the summer. The mortality rate is very low in comparison with the number of cases reported. The striking point in Table XI is that practically all of the deaths occurred outside of New York City where vaccination was enforced by a most efficient department of health.

TABLE X.—MORBIDITY FROM SMALLPOX IN NEW YORK STATE PER 100,000 POPULATION FROM 1915 TO 1925, ACCORDING TO MONTHS

Year	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1915.....	3.8	6.1	1.4	2.1	1.4	.5	.5	.1	.6	.7	1.6	4.
1916.....	.5	.4	.1	1.0	.8	.5	.2	.1	..	..	..	..
1917.....	.2	.5	.5	1.6	3.8	3.4	2.0	.5	2.9	11.3	3.5	12.4
1918.....	16.0	8.7	6.0	7.3	10.9	4.2	4.0	2.9	.6	.8	.6	.8
1919.....	1.7	1.1	1.4	3.2	3.2	1.3	4.3	.3	.7	.6	.7	3.5
1920.....	4.5	2.5	5.3	2.5	3.3	3.2	2.4	2.4	2.0	2.1	3.4	1.5
1921.....	6.7	8.5	17.0	11.6	8.2	10.1	3.8	4.0	1.5	.2	.5	.1
1922.....	.1	1.1	.1	.9	2.2	6.5	.3	.5	6.1	4.6	.6	5.5
1923.....	6.8	5.5	5.8	3.0	2.2	1.7	6.1	2.7	.7	.1	2.5	6.1
1924.....	2.1	5.6	4.1	1.4	4.5	4.3	3.0	1.1	1.3	3.6	17.3	5.5
1925.....	6.2	6.3	3.6	1.5	3.3	9.0	.5	.1	.1	..	.1	.3

TABLE XI.—MORTALITY FROM SMALLPOX PER 100,000 POPULATION OF THE UNITED STATES
DEATH REGISTRATION AREA OF NEW YORK STATE FROM 1915 TO 1925

Year	United States Registration Area	New York State	New York City	New York State Exclusive of New York City	Urban	Rural
1915	.3					
1916	.2	3		3		
1917	.3	4		4		
1918	.4	1		1		
1919	.4					
1920	.6	1		1		
1921	.7	1		1		
1922	.7	1	1			
1923	.1					
1924		3		3		
1925		2		2	1	1

Infective Period.—This disease is most contagious in the stage of invasion when the symptoms first appear, and lasts until the last scab has fallen off. The dry scabs contain the infectious material and are a source of danger. It is not communicable during the stage of incubation. The infectious agent may remain in cadavers for a long length of time and medical students have contracted smallpox in the dissecting rooms and morgue in this way.

Mode of Transmission.—The vast majority of cases are contracted from persons having the disease. As it is most contagious in the period of invasion even before the appearance of the rash, the possibilities of transmission to other individuals are very great. The disease may be so mild as to be unrecognized, yet such cases are as contagious as the more severe attacks. The contagion can also be carried through the body discharges of persons suffering from smallpox. It has been shown to have been carried on the clothing and by means of articles which have been in close contact with a patient. Flies and other insects can spread the contagion when they have been in contact with the patient's body or discharges. It can also be transmitted by a third person, so that nurses and physicians who are taking care of smallpox cases must use every precaution and surgical cleanliness.

It is believed that the virus enters the body through the mouth and nose.

It is improbable that this disease can be carried through the air and there is no trustworthy evidence to support this view.

SYMPTOMS

Period of Incubation.—This includes the interval between the entrance to the body of the virus of smallpox and the first tangible evidence of its presence by certain clinical symptoms. It is the period between the plant-

ing of the seed and the appearance of its growth and fertility in the soil. This period has been determined with a considerable degree of accuracy and it has been found to be from ten to twelve days in the cases which have been carefully studied. There are rare instances on record where the incubation period has been prolonged to twenty days. There are no signs of disease in this period and the child plays and goes to school as usual and no one suspects a dread disease is developing. It is the lull before a storm. Towards the end of this period the child may complain of headache, lassitude and perhaps a slight sore-throat.

Period of Invasion.—This is the initial stage of the disease and is usually ushered in abruptly with a chill or convulsion in young children. The first symptom is a chill which may be severe enough to cause the teeth to chatter. At the same time the temperature rises rapidly, ranging from 102° F. to 106° F. and in some cases as high as 107° F. Young children often have a convulsion instead of the chill. The elevation of temperature is sudden, and rises rapidly from normal to a high degree. Profuse sweating is apt to follow the chill. The pulse is rapid and corresponds with the temperature curve. The respirations increase with the fever and in normal and uncomplicated cases the three vital signs, fever, pulse and respiration, increase in the same ratio.

Headache usually follows the chill and may be very severe. Backache is a prominent symptom and occurs in nearly all the cases and is considered a diagnostic sign. It is found much more regularly in smallpox than in any of the other infectious diseases.

The head is flushed and the carotids visibly flushing. The prostration may be intense and out of all proportion to the length of the illness. The tongue is coated and the breath offensive, and vomiting is a frequent symptom in children. This vomiting may be severe and persisting and may continue for a couple of days. There is gastric pain and tenderness in the severe cases. The bowels are usually constipated. The entire body becomes tender, the muscles are sore to the touch and the knees ache. If the child attempts to sit up he will complain of vertigo.

Prodromal rashes which simulate measles and scarlet fever are not infrequent and make it difficult in sporadic cases to make a correct diagnosis.

The duration of the period of invasion is from two to four days and in many cases the fever becomes lower and a general improvement in all the symptoms takes place.

Period of Eruption.—Three or four days after the abrupt onset and when the symptoms have abated somewhat an eruption appears on the face and forehead and rapidly spreads to the scalp, arms and forearms. It shows early on the genitals and more slowly on the trunk and lower ex-

tremities. No portion of the body is exempt, and many lesions are seen at
the sites of the hair-follicles, sebaceous and sweat glands. In rare cases
the eruption is first noted on the trunk or extremities.

The eruption at first is macular and the spots may be so faint as almost
to escape notice. At first they are from the head of a pin to a pea in size.
The lesions rapidly increase in number and size and pass into the papular
stage. These are slightly elevated and give a characteristic "shotty" sensa-
tion on palpation. At this time the child appears much better, the fever
diminishes and the headache and backache disappear. The papules increase
in number and become confluent in severe cases.

On the third day of eruption the papules begin to fill with fluid and
become vesicles in twenty-four to thirty-six hours. Some papules become
vesicular before the general eruption and are diagnostic of smallpox. By
the fifth day all the papules have become vesicular and have about the size
and shape of a split pea. These vesicles are hard and firm to the touch,
even more so than the papules from which they developed. The color is
pink at first with a small areola of the same color surrounding it. As the
amount of exudation increases the vesicle takes on a shiny opalescent hue
somewhat like a pearl and gives a most distinctive appearance.

The contents of the vesicles become milky after the fifth day and a
central depression in each lesion appears. The lesion becomes flattened with
a dipping down in the center. This is called "umbilication." The periphery
of the vesicle frequently presents a bulging appearance and is typical and
characteristic of the disease. Umbilication does not take place in all the
lesions and in mild cases it is absent altogether.

The contents of the vesicles continue to become more turbid until they
are purulent. This is largely due to an increased exudation of leukocytes.
The lesions now become larger and more globular and the umbilication dis-
appears as the fluid breaks down the vertical partitions and forms one
cavity. This occurs on about the eighth day of the eruption. The pustules
remain intact unless scratched or broken. The color is yellowish-white like
ordinary pus. The areola becomes darker red in color and swollen and
raised. This swelling and redness may be so extensive on the face and
scalp as to render the features of the patient completely unrecognizable. The
loose tissue around the eyelids becomes edematous and so puffed as to com-
pletely close the eyes. This gives the child a revolting appearance, and a
patient in this stage presents a horrible spectacle. The inflammation of
the face and scalp is exceedingly painful and the patient dreads the pressure
of the pillow on his scalp and the bedclothes on his body. Schamberg made
a count of the number of lesions in one of his patients suffering from semi-
confluent smallpox. The results were as follows:

```
Total on fingers of one hand...............  392
        Thumb ............................   61
        Index finger......................   97
        Middle finger.....................   95
        Ring finger.......................   81
        Little finger.....................   58
Dorsal surface of one hand .............  382
Palmar surface of one hand..............  129
Total lesions on both hands................    1,806
Forearms ..................................    4,400
Arms ......................................    2,840
Chest .....................................    1,000
Abdomen ...................................      175
Thighs ....................................    4,180
Legs ......................................    2,850
Feet ......................................      750
Back ......................................    5,700
Estimated number on face and scalp.........    3,000
                                               ------
        TOTAL ............................   26,701
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He estimated that each pustule at the height of its development contained about three drops of pus, so that this patient must have carried about 5 quarts of pus in his skin. He has seen severe cases in adults having over forty thousand pustules. No wonder this disease is so fatal and was regarded with such horror when it was rampant. The fear exists even to this day when it is no longer a pestilence.

The patients in this purulent stage have a pungent and offensive odor which pervades the sick room and even the entire house.

The symptoms again become severe and distressing in the suppurative stage. The fever which abated with the appearance of the exanthem again begins to rise. This is termed the secondary or suppurative fever. While it may not equal the initial rise, yet it may reach as high as 104° F. This fever usually commences on the fifth or sixth day of the eruption and generally continues for three or four days, although in severe cases it is of much longer duration. The pulse and respiration in uncomplicated cases correspond with the temperature curve. The pain and discomfort are very great on account of the soreness of the skin and the pressure on the sensitive and inflamed pustules caused by lying or moving in bed. This causes sleeplessness and restlessness. The mental symptoms may be very pronounced, and delirium is not at all uncommon. There may be delusions and other signs of acute mental disturbance, and the patients have to be continually watched.

The mucous membranes are involved at the same time as the skin, and the enanthem may be observed before the exanthem, as is the case in measles.

It bears direct relation to the severity of the eruption on the skin. The lesions do not develop into papules, vesicles and pustules as on the skin, but may turn into superficial ulceration as is seen in aphthæ. The tongue is often involved and becomes swollen and sore, making it difficult to talk and eat. The throat is very sore in a large majority of the cases and is so inflamed that the child cannot take solid food. The enanthem appears on the mucous membrane of the nose and causes inflammation and the formation of crusts that make it difficult to breathe. This is especially distressing in nursing infants who have difficulty in nursing and taking the bottle on account of the impossibility of breathing through the nostrils.

The larynx often becomes inflamed in young children and they become croupy, and cases of sudden death from edema of the glottis have been reported. It is necessary in some cases to resort to intubation or even tracheotomy to prevent asphyxia. Acute dilation of the heart and collapse are noted at this stage.

Period of Desiccation.—This is first shown by the subsidence of the skin inflammation and the drying up of the pustules with the formation of scabs. This usually takes place about the eleventh or twelfth day of the eruption, while in mild cases it appears earlier. This desiccation does not occur simultaneously over all portions of the body but follows the sequence observed when the eruption first appeared. If the pustule has not been broken it will dry in the form of yellowish crusts. If they rupture, the centers will dry and sink in, giving a craterlike appearance to the lesion. This is called secondary umbilication. This differs from the primary umbilication in that it is larger, more craterlike and occurs at a later stage of the eruption. This is seen most often and most typically on the dorsal surfaces of the hands. The adherence of the scabs varies according to the involvement of the true skin. Where the pustule is merely superficial and not extending into the cutis the scab is easily detached, showing merely a reddened area of the skin. Those which extend into the cutis take longer to fall off or desquamate and leave the characteristic pitting or pock mark. This stage is accompanied by intense itching and it is hard to restrain a child from scratching and clawing the skin. This leads to bleeding and infection of the skin and subcutaneous tissue with pyogenic bacteria. Some of the pock marks are undoubtedly the result of such injuries. For some time after the desquamation the pock will be pigmented, and it is several months before the color of the skin returns to normal.

Now comes the period of convalescence when there is a marked improvement in the general condition of the little patient. The appetite returns, the weight increases and the child wants to be up and doing. At this time one can determine the extent of injury to the skin—whether the child will be deeply pock-marked for life or has escaped such disfigurement.

CLINICAL VARIETIES

Smallpox shows several distinct types which differ mainly in regard to severity and extent of eruption. Cases of true smallpox have been reported where there were but two or three papules present, while others may have a most profuse eruption covering the skin of the entire body. Between these two extremes there may occur intermediate forms. These may be classified as follows:

    I. Hemorrhagic—including variola purpurica and pustular hemorrhagic variola
    II. Confluent variola
    III. Discrete variola—including varioloid

I. **Hemorrhagic Form.**—This is the most severe and fatal of all forms of smallpox. The hemorrhages may appear as petechiæ during the stage of invasion, or small ecchymoses in the base or between the lesions. The vesicles may contain bloody fluid. The causative factor appears to exist in the individual's blood stream or blood-vessels. During the stage of invasion it differs little from other types until the petechiæ spots appear about the time the eruption is due. Hemorrhages occur in the mucous membranes and often in the conjunctivæ. The most dangerous and most malignant form is known as variola purpurica. The initial symptoms are very severe, especially the vomiting which is persistent and distressing. Purpura spots appear in the skin which later may enlarge and coalesce. This gives the face a dusky red and swollen appearance. The hemorrhages into the conjunctivæ are so profuse that the patient is unable to completely close his eyes. As the disease progresses the discoloration of the skin deepens and darkens so that this form is popularly known as black smallpox. These cases invariably terminate in death and the course is usually rapid and it rarely lasts over three or four days after the appearance of the eruption.

The pustular hemorrhagic form is less fatal and it is characterized by the hemorrhages taking place in the vesicles or pustules. If this takes place early in the disease the outlook is unfavorable. This may be limited in certain localities or extend over the entire body. This form is more apt to develop in old and debilitated persons and those addicted to alcohol.

II. **Confluent Variola.**—This is next in severity and danger to the hemorrhagic forms. The invasion is severe with persistent vomiting and nausea, severe headache and backache, high fever and convulsions or diarrhea. The high and continued fever is a prominent symptom. The eruption is profuse, especially on the face and arms, and the skin burns and itches. The coalescence of the lesions is often observed in the papular stage, but is more marked and more extensive when the pustules develop. They

may form large blebs filled with pus and when this exudes on the skin it produces a disgusting and disagreeable odor. The face and hands become swollen and edematous and the patient is unrecognizable. The suppurative process extends into the true skin and the crusts are much slower in dropping off. The disfigurement from the pitting is permanent. The constitutional symptoms during the pustular stage are severe and the fever again rises to a high degree. Many complications, such as cellulitis, empyema, keratitis, etc., are apt to develop. The mortality is high, but varies in different epidemics. The average mortality is about 50 per cent. When recovery results the convalescence is slow and tedious and is often complicated by the development of boils and abscesses.

III. **Discrete Variola.**—This includes the mild forms of smallpox. In some of these cases the initial symptoms during the stage of invasion may be as severe as in the confluent form. This applies to the headache, vomiting, backache and high temperature. The fever in the mild cases drops to about normal before the appearance of the eruption. The lesions do not tend to coalesce and are few in number compared with the confluent type.

The term *varioloid* is given to a mild form of smallpox which may occur in vaccinated persons in whom complete immunity was not established. The term is erroneous, as it is not a disease simply bearing resemblance to variola but is true smallpox, and unprotected persons who come in contact with these cases will develop true variola. These patients have very slight initial symptoms and may show only a single lesion on the skin. It is possible to go through the initial stage with a chill, fever, headache, backache, nausea and vomiting but remain free from eruption. To this mild form of the disease the term "variola sine exanthemate" has been given.

When the eruption appears it is milder in its course, exhibits many variations and is of shorter duration. The lesions become abortive and dry up early and as a rule do not extend into the true skin and do not leave a permanent scar.

There have been reported in recent years in different parts of the United States epidemics of mild and abortive cases of smallpox. The usual precautions not being taken on account of the mild character of the disease, the affection showed a tendency to spread all over the country. The cases retain their mild character and do not revert back to severe forms of smallpox. There is very little constitutional disturbance and there is no mortality. The period of incubation averages fourteen days, which is two or three days longer than smallpox. The symptoms in the stage of invasion are so mild that it is difficult to keep the child confined to his bed. The eruption is discrete but in some cases is rather copious and may be severe enough to become confluent on the face and to leave permanent pock marks. The

cycle of the eruption is shorter than in severe smallpox. The smallpox virus appears to be attenuated in virulence. The disease occurs exclusively among the unvaccinated and unprotected. One vaccination, no matter when performed, if it was successful will protect the individual. It is very contagious to unvaccinated persons. It is known by different names in different sections of the country as Cuban itch, elephant itch, impetigo contagiosa, etc.

A similar if not identical disease occurs in Africa and is called *alastrim*. This disease has a mortality of about 2 per cent and vaccination protects against alastrim. Rucker of the United States Public Health Service claims it is a mild form of smallpox and that under certain conditions it might regain its virulence and cause a highly fatal type of smallpox with much disfigurement. Alastrim is found in Egypt, the Soudan and the West Indies.

Smallpox in the Pregnant Woman.—The symptoms and course of smallpox are influenced by the state of pregnancy. The disease runs a more severe course and the mortality is high. Abortions and premature births occur in a large percentage of the cases and add to the gravity of the prognosis. This takes place in the majority of cases before the fifth day of eruption. The high mortality is shown in the figures of Schamberg, where twenty died out of twenty-seven cases in pregnant women who had never been vaccinated, giving a mortality of over 74 per cent. Of eighty-five women who had been vaccinated at some previous time fourteen died, showing a mortality of 16 per cent. This mortality varies in different epidemics but is always high.

Smallpox in the Fetus.—There are a few cases in the literature where mothers who had been protected by vaccination and never suffered from smallpox gave birth to babies with signs of smallpox. The mothers had been, however, exposed to variola. It would seem that the virus did not attack the immune tissues of the mother but may have reached the blood of the fetus and there multiplied. Mothers, on the other hand, who may develop variola at the end of pregnancy may give birth to a healthy infant who, unless immediately vaccinated, will develop the disease later. These infants seem, however, difficult to inoculate with vaccine virus. The writer observed a case of true variola in an infant whose mother did not have variola but who had been successfully vaccinated. The mother and infant were exposed at the maternity hospital to a case of smallpox that had been erroneously diagnosed as chickenpox. The baby was vaccinated but it did not "take" and a few days after came down with variola. There have been a number of similar cases recorded.

Smallpox may be communicated through the blood stream of the mother to the fetus in utero at any time after the fourth month. In the early months the fetus usually dies and the mother aborts. There have been cases in

which the fetus survived the attack and was born with typical smallpox scars. Lynn reports the case of a woman who became ill from smallpox in the eighth month of her pregnancy. One month later she gave birth to a baby who was covered with the eruption, and inoculation from the lesions resulted in typical variola. The fetus may die as a result of the mother's illness and be aborted without showing any signs of smallpox.

COMPLICATIONS AND SEQUELÆ

Boils and Abscesses.—Infection of the skin lesions with pyogenic organisms furnishes the most frequent complication. Few cases escape the discomfort of a crop of boils. These are usually superficial but may be very numerous. They develop most frequently after the pustules begin to dry up, which is after the twentieth day of the disease. Larger abscesses may develop in the deeper layers of the skin and are accompanied by cellulitis of the surrounding skin, and this may go on to gangrene. They may occur on any part of the body but are most frequently found on the scalp, face, arms and legs.

Carbuncles are sometimes seen during convalescence from this disease. Infection from streptococci is sometimes observed and causes high temperature accompanied by cellulitis which is often fatal. Bed-sores may add to the discomfort of the patient in severe cases and in debilitated patients. These are often the results of uncleanliness and pressure and can be avoided by skillful nursing.

The eruption which appears on the mucous membranes, called the enanthem, may become ulcerous and when they appear on the larynx in young children a spasm or edema of the larynx and glottis may develop which may lead to sudden death. The eyeballs are involved in severe cases with a resulting keratitis, perforation of the cornea, iritis, or hemorrhages in the conjunctivæ and even into the retina. The kidneys are frequently involved. Albuminuria is nearly always present in the early stages. It has but little significance unless complicated with an acute nephritis. There may be fatty degeneration of the liver and of the heart muscle in the more severe cases. The brain is congested and the autopsy reveals encephalitis in cases with marked delirium and mental disturbance. Inflammatory areas in the spinal cord resulting in paraplegia and other forms of myelitis have been observed.

DIAGNOSIS

In moderately severe cases this disease can be easily recognized during the pustular stage. In mild and atypical forms the diagnosis is not so easy. It is more difficult to diagnose in the initial stage before the appear-

ance of the rash, and as it is most contagious at that period it is important to make a correct diagnosis. The presence of an epidemic and of a known exposure will simplify matters. The mild cases and those modified by vaccination present great difficulties in diagnosis. Smallpox in a vaccinated person (varioloid) may be unrecognized, as there may only be a single papule present, but nevertheless such a case could transmit smallpox to an unvaccinated person. Unless there is a history of exposure it is not possible to make a positive diagnosis before the appearance of the rash. The existence of an illness with fever, backache, headache, vomiting, etc., preceding the eruption by several days should be considered very suspicious of smallpox.

Differential Diagnosis.—*Influenza.*—Practically all of the symptoms in the stage of invasion are duplicated in influenza. In the absence of an epidemic of smallpox the diagnostic sign would be an absence of rash by the fourth day. If no rash appears it would point to influenza.

The diseases which might be confused with smallpox after the eruption appears are measles, scarlet fever, chickenpox, roseola, acne, impetigo, etc.

Measles.—A measle-like prodromal rash sometimes appears in smallpox. There are no catarrhal symptoms and no Koplik spots are present. In the early days of medicine these two diseases were often confused and were grouped together by many writers of that time. Cases of measles occurring during an outbreak of smallpox are not infrequently sent to smallpox hospitals. The course of the temperature differs. In smallpox the temperature is highest at the onset of the symptoms and falls with the appearance of the rash. In measles it starts lower and rises with the outbreak of the eruption. There is a soft and velvety touch to the eruption of measles, while the papules in smallpox have a hard and shotty feel and in the course of twenty-four hours the measles rash becomes more diffuse and flatter while that of smallpox becomes more discrete and elevated.

Scarlet Fever.—The early occurrence of sore-throat and the distinctive strawberry tongue would point to scarlet fever even though a scarlatiniform prodromal rash is sometimes observed in smallpox which is accompanied by vomiting and high fever. The appearance of firm, hard papules and a little later the vesicles would remove all doubt of the diagnosis.

Chickenpox.—This is perhaps one of the most important diseases to be differentiated from smallpox, especially the mild cases in which there are no severe symptoms in the preëruptive stage. In chickenpox the papules do not have a shotty sensation and there is no secondary fever with the appearance of the pustules. The rash in smallpox is more abundant on the face and extremities and is most scanty over the chest and abdomen. It favors exposed portions of the body and is present on the palms of the hands in smallpox, while the opposite is true in chickenpox. The evolution of the

lesions takes about eight days in smallpox and three days in chickenpox. The lesions tend to become umbilicated in smallpox and rarely so in chicken-pox. There is very slight temperature in chickenpox and the course is short, and vaccination has absolutely no influence in modifying or preventing chickenpox.

Roseola.—A peculiar rash, possessing some similarity to smallpox, is sometimes seen in connection with vaccination but is distinguished by the fact that it always follows vaccination and is more macular than papular. It is never preceded by a high temperature or the symptoms observed in the stage of invasion in cases of smallpox.

Acne.—While the lesions on the face in mild cases of smallpox may bear some resemblance to acne, yet the absence of prodromal symptoms, or history of exposure and the progressive evolution of the lesions, would quickly clear up any doubt as to the diagnosis.

Severe pustular eczema of the face at first glance might suggest small-pox, but the history of the illness and the absence of lesions of the body and extremities would make the diagnosis clear.

Impetigo contagiosa is very frequent in children and shows various types of lesion. It may first appear as a papule which soon becomes vesicular and pustular. They enlarge and often appear in groups without previous symp-toms. Crusts form in a few days and the favorite location is about the mouth, chin and hands. There are no constitutional symptoms and no char-acteristic sequence or situation of the skin lesions as in smallpox.

PROGNOSIS

This depends on whether the patient has been vaccinated, the number of pustules, especially on the face and hands. The hemorrhagic and con-fluent types are the most virulent and few infants and young children re-cover from these severe forms. The age of the patient is important, as the mortality is very high in young persons. Children who are not protected by vaccination are very susceptible to contagion and are very likely to contract the more severe types of the disease. The virulence of the prevailing form of smallpox in an epidemic affects the prognosis. The characteristic pitting or scarring occurs in the severe cases and it cannot be avoided by any kind of treatment.

Nothing perhaps is so striking in the history of medicine as the effect of vaccination on the mortality from smallpox. For the past ten years the number of deaths each year from smallpox in the State and City of New York with over twelve million population averaged slightly over one death a year. A century and a half ago smallpox was the most frequent cause of death in young children. To-day, thanks to vaccination, it is negligible.

TREATMENT

Prophylaxis.—The first and most important step in prevention is vaccination. All contacts and every person who resides in the vicinity of a case of smallpox should be vaccinated at once. This procedure is required by law in several states. It is an established scientific fact that vaccination will effectively prevent the spread of smallpox. It is incomprehensible that in spite of this procedure smallpox is allowed to continue in civilized countries.

FIG. 2.—VACCINATION.
Three children of one family, the two older children protected by vaccination, while the unvaccinated baby contracted the disease.

Many people are opposed to compulsory vaccination on the grounds that it interferes with personal rights and liberty. The antivaccination adherents make all sorts of absurd and erroneous claims of dangers from inoculation of syphilis, tuberculosis and other diseases. This, of course, is impossible with the use of sterile bovine lymph. The technic and course of vaccination are described in a chapter devoted to that subject.

If vaccination of every child was made compulsory with revaccination as circumstances required there would be no need for other means of prevention. Municipalities and school authorities should furnish free vaccina-

tion to all children whose parents cannot afford to pay the services of a physician.

Sir William Osler some years ago made the following challenge: "I will go into the next severe epidemic with ten selected vaccinated persons and ten unvaccinated persons. I should prefer to choose the latter—three mem-

FIG. 3.—VACCINATION.
Two infants in an institution, one protected (right) against smallpox.

bers of parliament, three antivaccination doctors if they could be found, and four antivaccination propagandists. And I will make the promise neither to jeer nor to jibe when they catch the disease, but to look after them as brothers, and for the four or five who are certain to die I will try and arrange the funerals with all the pomp and ceremony of an antivaccination demonstration."

Notification.—Smallpox is a reportable disease and under the health laws of a number of states failure to notify the health officer of the existence of such a case is punishable by a fine. If a physician is in any doubt the opinion of some one familiar with the disease should be obtained. To report and quarantine a case as smallpox in which there has been an error in diagnosis is subjecting the household to much annoyance, inconvenience and unnecessary expense.

Isolation.—Every case should be isolated either in the home or at a special hospital. General hospitals cannot take care of cases of smallpox. Popular fear about smallpox has not been entirely effaced and so smallpox hospitals are available in most of the cities in this country. Unfortunately, the term "pest-house," which is a relic of the dark ages, is given these hospitals. Smallpox hospitals should be made available in any community where an outbreak of smallpox occurs. Such a hospital must be sanitary, with modern conveniences, and made as comfortable as possible for the patient. An ambulance should be part of the equipment and used only for smallpox patients and should be distinctively marked so the public may know the character of the disease it conveys. All nurses, servants and other employees must be vaccinated or revaccinated before entering upon duty.

If the child is to be treated at home a rigid and strict room quarantine must be enforced. A room with private bath separated from other parts of the house is desirable. Patients who live in small apartments or small houses are best cared for in a hospital. Needless furniture, such as upholstered chairs, carpets and draperies, should be removed. There should be ample ventilation. The attendants and nurses, who must be freshly vaccinated, should wear clothing that can be boiled, disinfected and laundered. Caps to cover the hair should be worn in the sick room. All discharges from the patient should be received in vessels containing chlorid of lime or carbolic acid. Discharges from the nose and throat should be received on old cloths or paper napkins and burned at once. Nothing should leave the sick room without previous disinfection. Visitors should not be allowed, but if they do go into the room they must take the same precautions as the nurses.

Physicians should be extremely careful not to carry the virus on their clothing or hands. The attending physician should have a long gown and cap which are hung in the open air between visits and should be frequently sterilized. It is a safe plan to wear rubber overshoes to avoid carrying dust or scabs which may be on the floor. These are kept with the gown. The hands and face should be washed after leaving the room and the hands held for a few moments in a disinfecting fluid such as bichlorid 1 :10,000, carbolic acid 1 :40, or lysol one dram to a pint. A physician should be vaccinated before taking charge of a case. If he is immune he will suffer no

inconvenience. A physician who frequently comes in contact with cases of smallpox once told me he had been vaccinated over fifty times and it had only "taken" twice.

Quarantine.—The question of what to do with the other members of the family when a case of smallpox occurs is a serious one. If the patient remains at home they should be quarantined and if they decide to leave the premises they should be vaccinated, change their clothing, take an antiseptic bath, and disinfect the hair. They should be kept under close surveillance by the health officer before they come in contact with others. Unless they are successfully vaccinated within three days of first exposure they must be kept under close watch for at least twenty days. If they are or have been successfully vaccinated they can be allowed their liberty, if in the opinion of the health officer it is wise to do so.

If the patient is removed to a hospital the room and house should be thoroughly fumigated and aired. After this has been done the other members of the household may be granted their freedom. It is desirable for them to be seen daily by a physician who should watch for symptoms of smallpox as well as the course of the vaccination.

Disinfection.—At the end of the quarantine period when the patient has entirely recovered his entire body should be washed and disinfected, his hair and scalp shampooed in a 1:10,000 or 1:20,000 solution of bichlorid. After this he puts on fresh undergarments and clothing which has not been exposed to the infection, or, if exposed, has been disinfected. Everything that has been in contact with the body of the patient should if possible be burned. If this is not practicable they should be boiled or immersed in a disinfecting solution for four hours. If the patient dies the body had best be disposed of by cremation, or placed at once in a metallic coffin hermetically sealed and buried without delay, and strictly privately.

The sick room should be disinfected as outlined above and then thoroughly aired, and the floors, walls and woodwork scrubbed with soap and water. The local and state health authorities have regulations regarding cleansing and disinfection which must be carried out under their supervision.

Medical Treatment.—The hygienic care of smallpox patients adds much to their comfort and chances of recovery. They should have fresh air in abundance with a temperature of about 70° F. Fresh air does not necessarily mean cold air, and in winter the air of the room can be changed frequently by opening the windows. The diet is of importance. During the stage of invasion with fever, vomiting and no appetite the nourishment should be liquid, such as broth, barley water, carbonated water, milk, etc. The patient should take as much fluid as possible. When the fever abates with the first appearance of the rash he should take as much nutritious food as he can digest to strengthen him for the great drain and strain during

the stage of suppuration. The diet should consist of milk, eggs, rare beef-steak, chops, etc., with as many of the well-cooked and easily digested vegetables as possible.

During the stage of eruption when the pustules develop and the second period of fever appears, a return to the liquid diet is necessary. The enanthem in the mucous membrane of the mouth, tonsils and pharynx causes great pain in chewing and swallowing. The appetite departs and it is difficult to administer any nourishment. The nurse should attempt to have him take small amounts of food every two hours. Milk can be given as plain, peptonized, buttermilk or lactic acid milk, junket, cooked with cereals, milk punch, custard, blancmange, etc. Eggs may be given cooked or raw in milk, etc. Alcohol should be used sparingly if at all in children. The diet can be greatly increased during convalescence. When the appetite fails to return, tonics containing strychnin and iron can be used.

Fever.—The best means of reducing fever in both the initial and suppurative stages is by means of cold sponging, the cold pack or by cold baths. This treatment is of benefit in controlling the delirium and mental symptoms which often accompany the high fever.

Pain.—The backache and headache in the initial stage are very severe and it is often necessary to resort to anodynes. Of these, antipyrin, phenacetin with or without codein, or even morphin may be necessary. Allonal is a safe anodyne for use in children. Local applications of counterirritants or heat should be avoided, as the eruption is always worse over such areas. Ice-packs or cold applications over the head often relieve the pain in the head. Children do not take opiates with the same degree of safety as adults, but in the painful stage of suppuration there is nothing so effective or so satisfactory as small doses of morphin.

The throat is a source of great discomfort and pain and it is very difficult to treat with applications or gargles, but argyrol or mercurochrome applied through the nose reaches the throat. Demulcent drinks, such as flaxseed tea sweetened and flavored with orange juice, are very soothing. When the inflammation reaches the larynx the use of inhalants is indicated. Steam vapor reduces the spasm. Compound tincture of benzoin, a dram to the pint, is helpful. If edema of the glottis develops the child is apt to suffocate unless a tracheotomy is performed.

The Eyes.—The frequent use of a boric acid eyewash in the early stages may prevent severe inflammation. White vaselin can be applied to the eyelids to prevent their sticking together. A few drops of a 10 per cent solution of argyrol or a 1 per cent solution of mercurochrome instilled in the eyes three or four times a day is indicated when there is much conjunctivitis. If an ulcer appears on the cornea, atropin should be instilled if the ulceration is central. If on the periphery, a drop of eserin sulphate, ¼ grain to the

ounce, should be used. The yellow oxid of mercury ointment should be used to prevent the denuded cornea from forming adhesions. The treatment of the eyes when involved must not be neglected and should be carried on both by day and night so as to prevent any permanent injury to the sight.

The Eruption.—The local application of antiseptics has been employed for many years. Ointments and greasy preparations should be avoided in the early stages. The itching and irritation is best allayed by wet compresses of boric acid, Dakin's solution, etc. Dusting powders are objectionable on account of their tendency to form crusts under which the suppuration is apt to extend. Compresses soaked in ice water and glycerin relieve the itching. Painting the confluent parts with a freshly diluted tincture of iodin is said to lessen the tendency of abscess formation and cellulitis. Spraying the lesions with ether and a 1 :5,000 solution of bichlorid has been recommended. The objects to be attained are to relieve the burning and itching, overcome the offensive odor, keep the skin clean, lessen the tendency to infection and prevent scarring.

For the itching, sponging with a weak carbolic solution, 1 :40, is sufficient in many cases. Spraying with alcohol with the addition of 1 per cent menthol is soothing.

Baths can be employed to prevent infection. Water containing 1 :20,000 bichlorid is effective, and it has the added value of reducing the temperature and quieting the delirium. Various antiseptics have been recommended, such as carbolic acid, creolin 1 :500, alum 1 :5 per cent, and potassium permanganate 1 per cent.

Many methods have been employed to prevent the scarring, but Schamberg says he has tried all of the much-vaunted measures without encouraging results. He obtained the best results by the application of pure or diluted tincture of iodin on the face twice a day. A hard parchment-like mask is formed which begins to crack and peel off. He then applies weak carbolized vaselin. The claim is that this treatment tends to shrink the pustules, to hasten decrustation, destroy the offensive odor and to some extent lessen the pitting. There is not so great liability to secondary pyogenic infection of the skin.

Potassium permanganate can be applied locally over the lesions and it is claimed to accomplish the same results as iodin.

No internal medication has any effect in modifying the course of the eruption.

The use of red light to exclude some of the chemical rays of light was strongly urged by Finsen of Denmark, but it has not given the results claimed by him. Ruhräh calls attention to the fact that the red light treatment was advocated by John of Gaddesden, a celebrated physician of the fourteenth century, who advised the use of red bedclothing, red bed curtains,

gargling of the throat with mulberry wine and the sucking of red pome-granates.

PUBLIC HEALTH REGULATIONS

Every physician must report at once to the local health officer every case of smallpox that comes to his attention within twenty-four hours from the time the case is first seen by him. This report to contain the full name, age and address. He must give detailed instruction to the nurse or other person in attendance in regard to the disinfection and disposal of the discharges from the nose, mouth and ears of the patient. It is the duty of the health officer if a suitable hospital is available to remove or cause to be removed such case promptly thereto. Every inmate of the household where such case occurs, and every person who has had contact with such case, or with his secretions or excretions, shall be either vaccinated within three days of his first exposure to the disease or placed under quarantine, and when vaccinated, the name and address of such inmate or other person shall be taken and such inmate or other person shall be kept under daily observation by the health officer. If no hospital is available the patient must be isolated and every member of the household shall be vaccinated or strictly quarantined until discharged by the local health officer. The minimum period of isolation is fourteen days after the development of the disease and until scabs have all separated and the scars completely healed.

Children must be excluded from school if the patient remains isolated at home until twenty days after the quarantine has been raised or seven days after successful vaccination and after disinfection of person if removed from quarantined premises.

If the patient goes to a hospital or children leave home when the disease is discovered no non-immune child shall be permitted to return to school until twenty-one days after removal or seven days after successful vaccination. An immune child is permitted to return to school.

The brief synopsis of the present status of smallpox as prepared by the committee of the American Public Health Association follows:

1. INFECTIOUS AGENT.—Unknown.

2. SOURCE OF INFECTION.—Lesions of the mucous membranes and skin of infected persons.

3. MODE OF TRANSMISSION.—By direct personal contact; by articles soiled with discharges from lesions. The virus may be present in all body discharges, including feces and urine. It may be carried by flies.

4. INCUBATION PERIOD.—Eight to sixteen days. (Cases with incubation period of twenty-one days are reported.)

5. PERIOD OF COMMUNICABILITY.—From first symptoms to disappearance of all scabs and crusts.

6. METHODS OF CONTROL

   (*a*) The infected individual and his environment

      1. *Recognition of the Disease.*—Clinical symptoms. Tests for immunity may prove useful.

      2. *Isolation.*—Hospital isolation in screened wards, free from vermin, until the period of infectivity is over.

      3. *Immunization.*—Vaccination.

      4. *Quarantine.*—Isolation of all contacts until vaccinated with virus of full potency. Daily medical observation of all recently vaccinated contacts until height of reaction is passed, if vaccination was performed within twenty-four hours of first exposure, otherwise for sixteen days from last exposure.

      5. *Concurrent Disinfection of All Discharges.*—No article to leave the surroundings of the patient without boiling or equally effective disinfections.

      6. *Terminal Disinfection.*—Thorough cleaning and disinfection of premises.

   (*b*) General measures

   General vaccination in infancy, revaccination of children on entering school, and of entire population when the disease appears in a severe form.

CHAPTER VII

VACCINIA AND VACCINATION

Definition.—Vaccinia is a disease that does not occur in human beings except after inoculation. It is an acute specific disease characterized by the appearance, at the point or points of insertion, of the specific virus of a skin lesion which appears first as a papule, then becomes vesicular, later a pustule and terminates in desiccation, leaving a permanent scar. This may be attended with a slight constitutional disturbance for a few days after the appearance of the papule. The great importance of this disease is the fact that it protects the individual from smallpox and confers an immunity for an indefinite length of time.

Synonyms.—Cowpox, kinepox; la vaccine; Impfpocken, Schutzblattern; vaccinia.

HISTORY

A tremendous array of articles and books has been written on this subject. Prior to the introduction of cowpox inoculation by Jenner in 1798 a number of writers advocated and practiced preventive inoculation against smallpox by means of virus taken from human beings suffering from smallpox. This was called *variolation*. While the inoculated persons generally had a mild attack of the disease, yet it was sometimes fatal and was contagious to others. It is interesting to note that on account of the dangers attending such inoculations the process of variolation was prohibited by the English Parliament and its employment declared a felony in 1740.

The fame of recognizing that inoculation with cowpox prevented a man from contracting smallpox when exposed is universally accorded to Sir Edward Jenner. Several observers had noted this fact prior to Jenner's discovery and had successfully employed inoculation. It is of interest to note that the first authentic record of such inoculation was performed by a farmer in 1774 on his wife and two young children. That an infection with cowpox protected the person from smallpox seemed to be more generally accredited among the laity than the medical profession. Jenner, while a medical student, started on his long series of investigations because of a chance remark by a farmer's daughter that she couldn't get smallpox because she had had cowpox. He made his first inoculation on a country boy, James Phipps, in 1796, and two years later submitted his observations to the Royal Society of Physicians, but the paper was refused "lest it should lessen the

reputation he had already gained." He then published the paper as a pamphlet entitled "An inquiry into the causes and effects of variolæ vaccinæ."

This pamphlet has brought everlasting fame to the author but even to this day there is bitter and bigoted antagonism to a simple procedure which has saved millions of lives and untold suffering among all peoples of the world. The practice of vaccination was introduced into many countries within a few years after the appearance of this pamphlet. To-day there is not a civilized or semi-civilized country in the world where this procedure is not only practiced but made obligatory by the authorities.

The extent of the ravages of smallpox and its high mortality are discussed in the chapter on smallpox. Statistics prove beyond any shadow of doubt the efficacy of vaccination. Before Germany established compulsory vaccination 66.5 of every 1,000 deaths were due to smallpox, and after the use of vaccination this fell to 7.5 per 1,000 deaths. This applies only to the mortality, and the morbidity figures are even more convincing. Epidemics in countries where there is strict compulsory vaccination are now unknown, but in England and in our own country where vaccination is not strictly enforced and the whims of conscientious objectors are respected, sporadic outbreaks occur at irregular intervals and the victims almost invariably are persons who have never been successfully vaccinated. A striking instance occurred some years ago in the practice of the writer when an outbreak of smallpox occurred in a small orphan asylum. There were forty-nine children under four years of age in this institution and only one had been vaccinated. The disease spread and the vaccinated child was the only one who escaped. There were fourteen adult attendants who had the care of the children and charge of the building. Of these all but one had been vaccinated. The unvaccinated nurse had a severe attack and all the others escaped. So the child and the adults who were protected by vaccination did not contract smallpox, and all the children and the one adult who had not been protected by vaccination came down with the disease.

The records of the Surgeon General's office show that the mortality rate for smallpox among the soldiers in the Union troops was 37.2 per cent and vaccination was not given to all the soldiers. During the World War vaccination was made obligatory, and presumably every soldier was vaccinated. The mortality rate for smallpox was negligible.

VACCINE VIRUS

The germ or specific organism which produces vaccinia has not been definitely identified. It probably does not belong to the class of microorganisms known as bacteria. Some authorities believe that the active agent in the virus is filtrable, others that it is not. It is possible, as some claim,

that it belongs to the class of protozoa. The vaccine virus, obtained from the vaccinia lesion when in the vesicle stage, is popularly known as lymph. This has a slightly alkaline reaction and contains epithelial cells, leukocytes and the as yet unidentified parasitic organism. This organism can also be obtained from the scab of a person who has been successfully vaccinated. Up to the past twenty-five years this was the source of the virus and the family physician usually had one or more scales in his possession taken from children whom he knew were healthy. At that time the human virus was considered to be better than that obtained from the cow or calf. There is no doubt but that in rare instances certain diseases and skin disorders could be transmitted by human virus and it was impossible to procure it under aseptic technic or to keep it sterile.

In view of these dangers the United States Government took control of the production of vaccine virus. It was found that the virus obtained from the vesicles produced after inoculation on healthy young calves was the safest and best. Human virus is no longer used. The Government allows the use only of young calves that are carefully examined and kept in quarantine for two weeks. They are then inoculated on the tender skin of the groin and belly under the strictest surgical precautions. When the vesicles appear the lesion is curetted and mixed with a 50 per cent solution of glycerin. It is then kept in cold storage, often below the freezing point, from two to twelve months, free from exposure to air and light. A bacteriologic examination is made every two to three weeks and when there are no bacteria present it is considered to be "ripe" and safe to use. In the meantime the calf from which the virus was taken is killed and a careful autopsy made to determine if it was free from all disease. The virus is injected into guinea-pigs to find if it is free from all pathogenic germs. Small ivory points are dipped into the material and allowed to dry, and the points then carefully protected or a small portion is drawn into capillary tubes which are immediately sealed. The virus is ready for use.

Attempts are now being made to produce a sterile virus, and Noguchi at the Rockefeller Institute has been able to grow it successfully on media prepared from the testicle tissue of bulls. The laboratory of the New York State Department of Health has prepared some very potent virus by this means. The next step in the production of vaccine virus will undoubtedly be its sterile preparation in the laboratory and not in the stable as is now the case.

TIME OF VACCINATION

The vaccination laws of Germany require infants to be vaccinated in the first year of life unless the child is ill or in poor health. Vaccination of infants is attended with less general reaction than in older children. This

affords protection to young infants and this is important, as when smallpox was prevalent the greatest number of cases occurred in young children. When smallpox appears in a locality all infants as well as young children should be vaccinated at once without any exceptions. If the smallpox is not prevalent and the child is poorly nourished or suffering from some constitutional disorder or skin disease it is best to postpone vaccination until he is in better physical condition. The writer had a case of smallpox in a three weeks old infant who contracted it in a maternity hospital from a patient thought to have chickenpox. When the diagnosis was established all the newborn infants were vaccinated without any bad effects.

TECHNIC

The process of vaccination should be considered a minor surgical operation and the strictest asepsis must be observed. The skin should be carefully and thoroughly cleansed. The area is washed with green soap and water with some friction in order to dilate the capillaries. The arm is then dried with sterile gauze or absorbent cotton. Some physicians scrub the skin with alcohol and then pour a little ether over the area.

The left arm is the classic and favorite site for vaccination. The place usually selected for the introduction of the virus is at the insertion of the deltoid muscle. There is a feeling on the part of many mothers that a scar on the arm

Fig. 4.—Vaccination.
Acupuncture method with needle through drop of virus.

is disfiguring and they object to this site for cosmetic reasons. A vaccination scar need not be large enough to disfigure and it should be considered a mark of honor—not of disgrace. A lesion on the inside of the leg may become irritated from the use of the leg from walking, or infected from the friction of the clothes and other irritations. Many physicians refuse to vaccinate on the leg on account of these severe reactions. Persons who insist on being vaccinated on the leg should be kept in bed from the time the papule appears until the formation of the scab in order to guard against a severe reaction.

The needle or scarifier should be sterilized by heat, or dipped in alcohol. Some manufacturers provide ivory or glass points which are sterile and require no further attention.

When everything is in readiness the skin of the arm is made tense by grasping the inner side of the arm with the left hand. The epidermis is gently scratched without going through the true skin and causing bleeding. A scratch not longer than an eighth of an inch is sufficient. It is most important not to bring blood, as it may wash away the lymph and prevent absorption. It is claimed by some observers that a deep scarification is more likely to be followed by a greater degree of inflammation.

FIG. 5.—VACCINATION.
Small scar affording immunity after acupuncture method.

A blunt instrument, such as a jeweler's screwdriver or a Pirquet scarifier, is very convenient as it will remove the epidermis without bruising the tissue and causing bleeding. It makes a very small point of entry, which results in a small scar which is invisible at a short distance. Some physicians vaccinate by an intradermal puncture with a hypodermic needle, employing a technic similar to making a Schick test for diphtheria. The United States Army method requires three long parallel scratches at least one inch in length.

It is quite essential to rub the virus thoroughly in the scarified area. The lymph should then be allowed to dry on the arm by exposure to the air.

J. P. Leake of the United States Public Health Service has suggested

FIG. 6.—VACCINATION.
Small scar which does not disfigure and affords complete immunity.

what he terms the "pressure" method and his description and directions as outlined in the United States Public Health Reports for January, 1927, are as follows:

A simple method is a shallow, tangential pricking of the cleansed but not irritated skin with a needle, through a drop of smallpox vaccine, covering an area not greater than one-eighth inch (3 mm.) in diameter. This gives little chance of accidental infection and the eruption is typical. The needle, which should be new, sharp and sterile, is not thrust into the skin but is held quite parallel or tangential to it, with the forefinger and middle finger of the right hand above the needle and the thumb below, the needle pointing to the operator's left. The needle should be crosswise of the arm, so that the thumb of the operator is not impeded by hitting the skin. The side of the needle point is then pressed into the drop about thirty times within five seconds, the needle being lifted clear of the skin each time. This rapid to and fro motion of lifting the needle and pressing it against the skin should be quite perpendicular to the skin and needle, and not in the direction of the needle. In this way the elasticity of the skin will pull a fraction of an inch of the epidermis over the point of the needle at each pressure so that the vaccine is carried into the deeper layer of epithelial cells, where multiplication takes place most easily. If the skin has not been unduly rubbed in cleansing, and if the motion is entirely perpendicular to the needle, no signs of bleeding will occur and all evidence of the punctures will fade out in less than six hours. Immediately after the punctures have been made the remaining virus is wiped off the skin with sterile gauze and the sleeve is pulled down, the whole operation of puncturing and wiping taking less than ten seconds. With strong vaccine a single pressure not infrequently gives a "take." Only six pricks or punctures were formerly advocated. Comparative tests showed this to be inferior to the scratch method in the percentage of successful "takes." By the use of thirty pricks, this difficulty has been overcome and the percentage of "takes" is as high as with any other safe method.

The disadvantages of this method, which it shares with some other methods, are, first, that without demonstration and practice the technic of applying the proper pressure may not easily be acquired, and, second, that without due care an area larger than one-eighth inch (3 mm.) in diameter may be covered by the insertion. In regard to the first point, the difficulty is usually that the needle is not pressed in the right direction or that the pressure is not firm enough. Provided the needle is held quite tangential to the curve of the arm, and the direction of motion is quite perpendicular to the needle, it is difficult to make the rapid pressure too firmly. In regard to the second point, motion from the wrist with the arm held rigid is usually more accurate than whole arm motion.

The advantages of the method are its mildness and painlessness, the fact that it is more rapid than any other effective and safe method, the fact that no control site is necessary since the evidence of trauma due to the operation has disappeared before the first observation for an early reaction is made, and the fact that the virus is wiped off immediately, so that the uselessness of a dressing is obvious to the person vaccinated.

Thomas and Bull gave this a thorough trial on the students of Lehigh University and have adopted it as the most efficacious and most satisfactory

method. It can be performed more rapidly and with less discomfort to the patient and it does not require the use of any dressing following the vaccination.

The *after care is important.* Nearly all of the "bad arms" and infections are the result of negligence and improper care. The consensus of opinion is opposed to the use of "shields" of any form or shape. These constrict the capillary circulation around the wound and keep the lesion too warm and too moist, making an excellent incubator for the growth of bacteria. The simplest and the safest dressing is several thicknesses of sterile gauze used as a covering. This can be held in place by one or two narrow strips of adhesive plaster applied at least an inch distant from the point of vaccination. The gauze should simply cover the lesion and not go clear around the arm. Like any other wound, proper care and surgical cleanliness must be followed until the wound is entirely healed.

FIG. 7.—VACCINATION.
Old-time scar (3.2 × 2.8 cm.) from butchery done about 1904 by "cross hatch" method.

The vesicle should be protected from injury, especially from scratching. The finger nails are sure to carry infection. If the itching is unbearable at night the application of a 50 per cent solution of alcohol over the inflamed area, but not over the lesion, or a small ice-bag placed over the point of vaccination will give relief. Gentle rubbing at a little distance from the lesion will give comfort.

The vaccination sore and the blister should be kept dry. If not, the fluid from the vesicle will adhere to the gauze and the scab will be torn off with its removal. When this occurs the wound can be washed with boric acid solution and thoroughly dried with sterile cotton, and boric acid dusting powder applied. It is a wise procedure to change the gauze dressing very gently each day and keep the wound dry with the use of an unscented sterile dusting powder.

The scab should be allowed to fall off. This happens when the surface under the scab has healed. If it is torn off it exposes a raw surface which is apt to become infected and the period of inflammation is prolonged and the resulting scar is larger.

SYMPTOMS AND COURSE OF VACCINIA

The length of time between the introduction of the virus and the first local symptoms depends somewhat on the virus, its source and its preparation. For two to three days after vaccination nothing is observed except the slight abrasion of the skin by the inoculation instrument, and it may be ten days before any redness is detected about the site of inoculation. This redness increases in size and color, and a distinct round hard papule appears. After a couple of days this papule becomes vesicular and this is usually observed along the margin of the inoculated area. The vesicle or vesicles increase in size and contain clear watery lymph. The vesicle becomes more elevated and reaches its height about the eighth day. The center becomes depressed or umbilicated and the periphery bulges and is more prominent. Jenner gave an accurate description of the vesicle "which has an appearance not unlike a grain of wheat with a cleft or indentation in the center."

At this time there appears a distinct inflammatory circle around the vesicle. This is called the areola and often extends for several inches around the lesion, gradually merging into the normal skin. This areola has been attributed to the reaction of the antibodies to the growth of the vaccine organisms. The lymph-nodes in the vicinity of the lesion and in the axilla are frequently enlarged and may be quite painful.

There are generally some constitutional symptoms about this time. Slight chills occur with a little elevation of temperature, the sleep is disturbed and restless and there is apt to be loss of appetite and malaise. These symptoms rarely last over a day or two. One cannot describe these symptoms more accurately or vividly than Jenner, who said: "On the seventh day he (a boy eight years of age) complained of uneasiness in the axilla, and on the ninth day he became a little chilly, lost his appetite and had a slight headache. During the whole of this day he was perceptibly indisposed and spent the night with some degree of restlessness, but on the following day he was perfectly well." The severity of these symptoms varies in different children and may be negligible or very severe.

On about the twelfth day after the appearance of the papule the lesion begins to fade and the contents become purulent. The scab formation starts in the center and the areola becomes smaller and shades off into two or three circles which vary from a pale pink to a deep red in color.

The surrounding tissue becomes normal about the fifteenth day of the lesion and desiccation is completed. The scab itself may not fall off for a week or two later.

The lesion passes through the stages of papules, vesicles, umbilication and pustules.

The dried crust is hard and of dark mahogany color and quite rough on

its surface. After it falls off the scar appears at first smooth and red, and after a few months becomes paler than the surrounding skin. It is usually pitted and has the appearance of being punched out with a sharp die. The center may become elevated and even keloid in character. Such scars remain red for a long time.

A slight leukocytosis appears three or four days after vaccination, which lasts about five days. A secondary increase in the number of white cells is found from two to three weeks after vaccination, which lasts about a week unless some complication arises.

False or Spurious Vaccination.—This occasionally occurs, and may lead to some confusion. It may appear in several forms. In one the papule appears on the second or third day and may develop into a small vesicle and quickly dries up and does not leave a scar. It never shows the umbilication or the scab formation. Another form is known as the raspberry excrescence on account of its appearance. The lesion is slightly raised, bright red in color and never goes on to the vesicular stage. It looks like a small capillary nevus and may remain in this condition for several weeks. No areola forms around the lesion and it is not followed by a scar.

Insusceptibility to Vaccinia.—Some people claim they have been vaccinated a number of times and it has never taken. There may be some cases of natural immunity against vaccinia, but they are very unusual. It is possible that a person may be immune at one time but later develop a susceptibility to vaccinia. The reasons why a vaccination did not take may be on account of faulty technic or impotent vaccine. If the first vaccination is not successful it should be repeated two or three times.

REVACCINATION

Immunity after vaccination may in a few cases last throughout life, but in the vast majority of cases it does not last more than ten years. Jenner at first believed that one successful vaccination protected for life, but changed this view later as his experience increased. There is no question but that the protective power of vaccination diminishes with the lapse of time. A wise plan is to vaccinate in early childhood and again at puberty. The popular idea of vaccinating every seven years is not scientific. In the presence of an epidemic or after exposure vaccination should be done at once. Many physicians believe that when a vaccination takes the person is susceptible to smallpox and that when it does not take he is immune. It is not safe to rely on this and after exposure to smallpox vaccination should be repeated if it fails to take.

The condition of the scar gives some indication of the protection of the individual. A good excavated scar in a person shows he is well protected.

It is claimed by the advocates of multiple inoculation, that is three or more scarifications, that the increased number of scars will prolong immunity. The size of the scar is believed by some to be indicative of the degree of protection. None of these theories have been successfully proved, and it is the character of the scar rather than the number or size that is important.

COMPLICATIONS

Any open wound presents possible dangers of infection. Besides, vaccinia is an infectious disease and there is always the possibility of systemic involvement even in the mildest diseases of this character. But the claims of the antivaccinationists are grossly exaggerated and distorted in the effort to create public sentiment against this humane and harmless procedure. We know that an insect bite or a pinprick will open the way for an infection which may result fatally. It is quite probable among the millions of persons throughout the world that there are some in whom the vaccination preceded some illness with which it had absolutely no connection. Such instances are greedily seized upon by the enemies of vaccination and given wide publicity. Tuberculosis, skin diseases and syphilis may show their initial symptoms shortly after a person has been vaccinated, and yet the vaccination is blamed by ignorant persons. Vaccination only protects against smallpox, not against any other disease or disorder.

Infection of the lesion can be avoided by proper care, and as the lymph now used is bovine prepared under Government supervision and control, the dangers are very slight. It can be absolutely stated that the infections and fatalities which occasionally occur after vaccination are avoidable and preventable.

Tetanus.—This is one of the most important infections. No one denies that it may and does occur, but its occurrence is rare. Cases of tetanus after toy pistol wounds greatly outnumber those from vaccination. In ten years only forty-one authentic cases of tetanus were found in over thirty-one million vaccinations. In the year 1910 there were 1,373 deaths from tetanus in the United States registration area and of these there were only sixteen, or about 1 per cent, which were claimed to have been the result of infection through the vaccination wound. John F. Anderson, formerly of the United States Public Health Service, inoculated monkeys and guinea-pigs with vaccine virus which had been contaminated by tetanus bacilli and found it to be impossible to communicate tetanus in that manner.

Tuberculosis.—It is almost impossible to introduce tuberculosis through a small and superficial skin abrasion. No case of a tuberculous node on the site of a vaccination lesion has ever been reported. It is extremely doubtful if any form of tuberculosis has ever been inoculated in this manner, and it

has never been proved that the reaction of vaccination has ever made active a latent tuberculosis. The glycerin which is used as the vehicle for the lymph has the property of destroying bacteria.

Skin Diseases.—These are usually the result of local infection through the wound, and the most dangerous are the streptococcus infections which used to be classified as erysipelas. The most common skin involvement is impetigo and this may spread and be transferred by the fingers to other parts of the body. A number of cases are on record, when a nurse or adult has had multiple vaccinations, on the face, in the nose, etc., from a scratch of a child whose nails were contaminated from a lesion on his own arm or by carelessness on the part of the adult. Eczema, urticaria, furunculosis may occur with vaccination or be lighted up by it, but are not in any way due to the virus of vaccinia. The modern aseptic technic and the strict preparation of the lymph have greatly reduced the number of infections.

PUBLIC HEALTH LAWS

Vaccination is a public health measure and is for the protection of mankind from the scourge of smallpox. In the United States each state enacts its own vaccination laws, and the opposition of the antivaccinationists and the strong political pressure they are able to exert in different states make a uniform nation-wide law impossible. The Government regulates the production of the virus and has a slight control over vaccination through the regulation of interstate traffic. Vaccination is compulsory before entering all branches of military service and in the Government civil appointments.

The Public Health Law of the State of New York can be cited as an example of present-day legislation concerning vaccination:

§ 310. *Vaccination of school children*

1. A child or person not vaccinated shall not be admitted or received into a school in a city of the first or second class. The board, officers or other person having charge, management or control of such school shall cause this provision of law to be enforced. The board of health or other board, commission or officers of such city having jurisdiction of the enforcement of this chapter therein shall provide, at the expense of the city for the vaccination of all pupils of such school whose parents or guardian do not provide vaccination for them.

2. Whenever smallpox exists in any other city or school district, or in the vicinity thereof, and the state commissioner of health shall certify in writing to the school authorities in charge of any school or schools in such city or district, it shall become the duty of such school authorities to exclude from such schools every child or person who does not furnish a certificate from a duly licensed physician to the effect that he has successfully vaccinated such child or person with vaccine virus in the usual manner or that such child or person shows evidence by scar of a successful previous vaccination. Whenever school authorities having the charge, management and control of schools in a district

or city cause this provision of law to be enforced, the local board of health shall provide for the vaccination of all children whose parents or guardian do not provide such vaccination.

§ 311. *Vaccination how made; reports*

1. No person shall perform vaccination for the prevention of smallpox who is not a regularly licensed physician under the laws of the state. Vaccination shall be performed in such manner only as shall be prescribed by the state commissioner of health.

2. No physician shall use vaccine virus for the prevention of smallpox unless such vaccine virus is produced under license issued by the secretary of the treasury of the United States or under a certificate of approval issued by the state commissioner of health, and such vaccine virus shall then be used only within the period of time specified by the expiration date.

3. Every physician performing a vaccination shall within ten days make a report to the local health officer upon a form furnished by the state commissioner of health setting forth the full name and age of the person vaccinated and, if such person is a minor, the name and address of his parents, the date of vaccination, the date of previous successful vaccination if possible, the name of the maker of the vaccine virus, the lot or batch number of such vaccine virus and whether upon reëxamination after a proper interval such vaccination was found to be successful or non-successful.

Sherman gives the following résumé of the regulations concerning vaccination in different countries:

England.—The first vaccination act, which was passed in 1840, made the operation of vaccination entirely voluntary. In this law inoculation with smallpox, or variolation, was forbidden and made a penal offense. In 1853 a compulsory vaccination law was enacted which required that all infants should be vaccinated with human lymph before three months of age. In 1867, an act was passed enjoining and encouraging revaccination. In 1898, bovine vaccine virus was designated to take the place of human virus; domiciliary vaccination was designated in place of vaccination stations; the period of infantile vaccination was changed to the age of three to six months; and the so-called "conscientious objector" clause was included.

France.—In 1902, a law was enacted compelling vaccination during first year of life and revaccination both at 11 and 21 years of age. Three inoculations were deemed necessary for successful vaccination; the use of bovine virus was advised. All conscripts to the army were revaccinated.

Germany.—In 1874, a law was passed compelling vaccination during the first or second year of life and revaccination at 13 years of age. This law required that the abraded area for vaccination should equal one-half of a square inch. Two inoculations were necessary, and inspection was required between the sixth and ninth day after the operation. Smallpox has thereby been virtually eradicated and epidemics are unknown.

Austria.—The earliest regulations which were introduced in 1808 amounted to but little. In 1900 indirect compulsion was enforced. Now all must be vaccinated before they enter schools, offices, public institutions or military service. As regards schools, however, the law can easily be evaded.

Russia.—Vaccination has never been made compulsory by a national act, but has, however, been in force indirectly, since without successful vaccination, one is forbidden entrance to schools, universities, civil or military service. Russia is a badly vaccinated country generally, and smallpox epidemics are not uncommon.

Italy.—Compulsory vaccination within six months of birth was required by law in 1888. If the primary vaccination fails, revaccination is obligatory within one year. These laws are strictly enforced.

Switzerland.—In 16 cantons, vaccination is compulsory, while in the remaining nine, it is discretionary. In these nine cantons, however, it is enforced indirectly, being necessary before entrance to school or official life. Revaccinations between 12 and 13 years is obligatory.

Norway.—Vaccination is not compulsory by law, but is compelled indirectly through school, university, army and navy regulations.

Sweden.—Compulsory vaccination by the end of the second year with six to eight vesicles, is enforced.

CHAPTER VIII

WHOOPING-COUGH

Definition.—Whooping-cough is an acute, highly contagious disease characterized by recurring attacks of spasmodic cough. The cough is of reflex origin and is a series of explosive efforts to dislodge an irritant in the trachea. Each paroxysm ends with a prolonged and peculiar inspiration causing a whoop and the expulsion of mucus.

Synonyms.—Pertussis, hooping cough, chin cough; Keuchhusten, Stiel-chausten; coqueluche; tossferina; pertossa.

HISTORY

No mention of this disease is to be found in the writings of our ancient medical forebears. The distinctive cough seemed not to attract their attention, or else the disease as we now recognize it did not exist. The first reference to this cough forming a distinctive clinical entity is found in the works of Baillon or Ballonius, a French physician who was born in Paris in 1538. He has been called the first epidemiologist of modern times. One of his most important contributions is the description of whooping-cough which appeared in 1578 when he was forty years of age. John Ruhräh in his *Pediatrics of the Past* refers to him as a remarkable character who deserves to be rescued from the comparative oblivion into which he seems to have fallen. A few extracts from his account of the disease are well worth reading to-day and may take away some of the conceit we may possess of the present-day monopoly of clinical medicine. "Especially that common cough, which is generally called quinta or quintana. Its symptoms are serious. The lung is so irritated that, in its attempt by every effort to cast forth the cause of the trouble, it can neither admit breath nor easily give it forth again. The sick person seems to swell up and as if about to strangle holds his breath clinging in the midst of his jaws. . . . for they are free from this annoyance of coughing sometimes for the space of four or five hours, then the paroxysm of coughing returns. Very frequently the belly happens to be upset. I have not yet read any author who writes about this cough."

Thomas Sydenham in 1670 mentioned the immense relief of venesection in infants in "pertussis or the whooping cough." An almost unknown

Swedish physician, Nils Rosen von Rosenstein, published a volume of lectures on children's diseases about 1766 in which appears the following: "The hooping cough, like the smallpox, measles and the venereal disease, never appeared in Europe originally, but was transported thither from other parts of the world by means of merchandise, seamen and animals; it was a new disease to our ancestors in Europe, and probably was conveyed to them from Africa or the East Indies, where it was noted before. Its first appearance in Sweden cannot be determined with any certainty; but in France it began in the year 1414. It is likewise observable that the hooping cough always appears as an epidemical disease. . . . I knew the hooping cough conveyed from a patient to two other children by means of an emissary. I have even myself carried it from one house to another undesignedly. A person who has once had the hooping cough is as secure from the danger of catching that disorder as those who have had the smallpox and measles are with regard to those respective diseases. During my practice I never found or heard of any one who has been infected with the hooping cough more than once. . . . for the disease is both tedious and severe. When it is left to the course of nature alone to be worked out, it will commonly last eleven or twelve weeks, nay frequently half a year. What is still worse the disease is very dangerous and often fatal."

Few modern writers have contributed any important facts about whooping cough since the descriptions quoted above. This disease has received much study and many theories of its causation have been advanced. There is not space to outline these theories, some of which were fantastic and the object of much controversy. No light was shed upon these disputed theories until 1906 when the specific organism was discovered by two French scientists—Bordet and Gengou. The work of these men has been confirmed by a large number of investigators.

ETIOLOGY

To-day no one questions the rôle of the Bordet-Gengou bacillus as the specific etiologic factor in whooping-cough. This organism is a small, short, oval, non-mobile bacillus which resembles the influenza bacillus in several points. It varies in size and is found usually singly or in pairs and rarely in short chains. It is Gram-negative and with appropriate stains bipolar staining. It is aërobic and facultative anaërobic. It grows best on the medium used by Bordet and Gengou, namely, glycerin, potato and blood agar, but will grow on other media when transplanted. This organism was first described in 1900 but a full report containing an intensive study was published in 1906.

This organism, which is also known as the *Bacillus pertussis,* is present

in large numbers between the cilia of the epithelium lining the trachea and bronchi. It is difficult to obtain the organism in the first mass of mucus brought up after the paroxysm of coughing. The later mucus is more apt to contain it, as it develops chiefly in the lower respiratory tract. It is most abundant in the early or catarrhal stage of the disease and is rarely found after the typical paroxysms or whoop appears. Smears are very unreliable and only cultures on the medium referred to above are to be depended upon. Chievitz and Meyer recommend opening a Petri dish containing the proper medium in front of the child's mouth when he is coughing as a simple method of obtaining the specific organism. In practically all cases there is a mixed infection usually with the influenza bacillus, hemolytic streptococcus, pneumococcus and staphylococcus. The methods of identification of the specific organism from the sputum will be discussed under diagnosis.

Predisposition.—The greatest susceptibility is found among young children from six months to five years of age. No age is immune and newborn babies if exposed to the disease are very apt to contract it. The writer has records of four infants under three weeks of age who contracted the disease from mothers who were in the catarrhal stage of the disease at the time of birth. It may occur at all ages and is not uncommonly seen in old age. It is generally agreed, however, that one attack confers immunity. Reported instances of second or third attacks can be explained by errors in diagnosis, and one not infrequently finds one of the parents develops a paroxysmal cough while their children are in the midst of an attack which is simply a sympathetic or nervous cough and is not contagious. There can be no question as to the great susceptibility of young children to whooping-cough and it is only equaled by that of measles. Biedert reported that of 401 children exposed during an epidemic in a village in Germany 366 or 91 per cent contracted the disease.

The disease is spread chiefly from droplets from the mouth and nasal spray from coughing, speaking or sneezing. Close proximity to the patient is not necessary and the infective distance has been placed at 5 feet by some observers. This contact can take place out of doors as well as inside the house. There is no question but that the disease may be carried by a third person or by articles which have been contaminated by the secretions of the throat and nose after coughing. Pencils, spoons, toys, cups, dishes, towels, handkerchiefs or any article recently soiled by a patient are often the means of transmitting the infection. The disease can only be spread in the early stage when the Bordet-Gengou bacillus is present in large numbers in the sputum.

The disease occurs most frequently in the winter months and early spring. It is world wide in its distribution. No country, race or climate

seems to be immune. It is a noteworthy fact that the negro has a much higher mortality than the white race.

Sex.—All the statistics of this disease in different cities, in different countries and in different years show that girls are more susceptible than boys both in the number of cases and in the number of deaths. This is the only infectious disease in which there is such a marked and constant predominance of cases among girls. No satisfactory explanation has been advanced. Some attribute it to certain anatomical differences in the throat and larynx, while others believe it is due to the greater susceptibility of the nervous system in the female. The incidence of cases among girls is 56 per cent as compared to 44 per cent in boys. Mortality statistics on whooping-cough covering a period of twenty-nine years show 108 deaths in girls to 100 in boys in the first year of life, 114 deaths in girls to 100 in boys in the second year, and this ratio increases as the age advances.

PATHOLOGY

Mallory of Boston who has made a number of investigations on the pathology of this disease claims that the specific lesion is the presence of the Bordet-Gengou bacillus between the ciliæ of the cells of the trachea and bronchi. There is a catarrhal inflammation of varying intensity affecting the mucous membranes of the upper air passages. If the attack has been protracted the lungs will show various degrees of emphysema. Other lesions of the lungs and bronchi are due to complications, the most frequent and dangerous of which is bronchopneumonia. If the child dies during a paroxysm the brain is congested and may show many punctate hemorrhages. The same conditions are found if the child dies during a convulsion.

SYMPTOMS

The course of the disease can be conveniently divided into three distinct stages: The catarrhal, or stage of invasion; the paroxysmal, or spasmodic stage; the stage of decline or defervescence. Atypical cases are found as in any well-defined disease and these different stages may not be sharply defined.

Incubation.—It is difficult to determine the exact duration of the period of incubation. The onset is very gradual and the early symptoms unnoticed. In cases where a careful watch has been observed this period seems to be from seven to fourteen days. It is comparatively safe to assume that if, after a direct exposure, the child does not develop a cold or a cough the probabilities are strong that the disease has not been contracted.

The period of infectivity is not definitely settled. The bacilli can only be

found in the sputum during the early stage of the disease, although there is plenty of clinical proof to show that children in the paroxysmal stage transmit the disease. It should be borne in mind that the catarrhal stage is the most contagious and that after the whoop is well established the infectivity rapidly diminishes.

The Catarrhal Stage.—The onset of this first stage is gradual and usually starts as ordinary cold with a coryza and cough with the palate and pharynx slightly reddened. There may also be a slight remittent fever. The eyes may be congested. The cough is dry and irritable and is much worse at night. This gradually increases in frequency and severity instead

FIG. 8.—SERIES SHOWING STAGES IN PAROXYSMS OF WHOOPING-COUGH.

of abating as in an ordinary cold. All physical signs of bronchitis are absent. In a few days attacks of coughing come on in paroxysms which at first are mild and only occur two or three times a day. They become more frequent and intense until the typical whoop develops which marks the beginning of the paroxysmal stage. Abt states that in the later period of the catarrhal stage the children tend to become less active and physically quieter because they learn that activity produces more frequent and more severe coughing spells. This first stage, therefore, is characterized by symptoms of a mild grade of respiratory catarrh involving the eyes, nose, pharynx and larynx often accompanied with a slight fever. This stage usually lasts from seven to fourteen days, although individual cases show considerable variation.

The Paroxysmal Stage.—This second stage is ushered in when the cough is so severe that the child loses his breath, becomes blue in the face and the typical and characteristic whoop is heard. The catarrhal symptoms disappear and between the attacks of coughing the child appears normal and in good health. A child can usually tell when a paroxysm of coughing is coming. He will run to his mother or seize some object for support. Older children often describe a sensation of choking or of a sense of constriction about the chest. The terror of some children preceding or during one of these attacks is distressing. A series of ten to fifteen short explosive coughs come on in such rapid succession that the child cannot catch his breath between them. The eyes water and seem to protrude, the face becomes congested and purple and the tongue puffed and bluish. Then a sudden rush of air through the narrow glottis produces a loud and crowing sound known as a whoop. Immediately there is a repetition of the cough followed by another whoop. In a severe paroxysm lasting from two to five minutes a child may whoop a number of times until a small amount of thick and sticky mucus is expelled. Epistaxis sometimes occurs with a severe paroxysm, but usually this is not severe or dangerous. Vomiting is almost certain to occur in young children, especially if food has been taken recently. Involuntary evacuation of the bowels or bladder often occurs during an attack. These attacks are more frequent at night and occur more often in a close room than in the open air. The number varies according to the severity of the case from five to fifty in twenty-four hours. They may be induced or increased in frequency by taking food, overeating or drinking, crying, coughing, sneezing, emotional disturbances such as fright or anger, or even by hearing some one else cough. Children are prostrated after a severe attack and are hardly able to stand alone. Death from asphyxia during an attack rarely occurs, although it may result from a cerebral hemorrhage.

There are mild cases in which no characteristic whoop develops, but the cough comes in paroxysms and is spasmodic in character. The cough continues until the mucus is expelled and the congested face and watery eyes are typical of whooping-cough. If bronchopneumonia develops the character of the cough will change and the whoop often disappears only to reappear when the pneumonia clears up.

Observers are not in unity regarding the seat of the irritation which produces the cough. Some claim it is the nose, others the trachea, the larynx or the bronchi. It is very possible it may vary in different cases. Laryngoscopic examinations made during the disease reveal a swollen and congested larynx. A collection of mucus can be seen in the trachea or on the posterior laryngeal wall just before the attack begins. It is claimed that this collection of mucus is the exciting cause of the paroxysm which continues until this is dislodged.

Between attacks the cough may be absent and the child appears well and happy. Hemorrhages in the conjunctivæ or in the skin may result from the severity of the cough. Examination of the chest during a paroxysm may show a temporary emphysema but between attacks there are no physical signs in uncomplicated cases. The duration of the attacks varies from a few seconds to five or ten minutes and the number varies from five to over fifty in twenty-four hours.

The average duration of this stage is about six weeks and may last twelve weeks. It increases in intensity for the first few weeks, remains stationary for one or two weeks and then gradually shades into the next stage. After it has entirely ceased the whoop may return with violence with a cold or attack of bronchitis. In some children the whoop returns with every cold for six months or a year after the original attack. This is not a relapse of the whooping-cough and is not contagious to susceptible persons. The stage of decline or third stage of the disease is characterized by a diminution in the number and severity of the attacks. The whoop disappears and the cough resembles that of a slight bronchitis. If any fever develops it is a symptom of some complication. The cough can revert to the paroxysmal character if the child catches cold or is emotionally excited. The whoop may return months after the cough has entirely disappeared. This stage ordinarily lasts from one to three weeks.

Atypical Forms.—In widespread local epidemics or in institutions where there is an outbreak of whooping-cough it is not at all rare to find cases with severe paroxysmal cough without the distinctive whoop. These cases are sometimes very difficult to recognize and keep under control and probably are responsible for spreading the infection. Some cases are accompanied by attacks of sneezing throughout the course. The catarrhal stage may be so slight that it is not recognized and the paroxysms seem to appear at the outset of the disease. This is more apt to be the case in very young infants.

The average duration of the disease in uncomplicated cases varies between eight and twelve weeks. Various factors can prolong each of the several stages. Not only climatic conditions but careless conduct in the management and treatment, severity of the infection, the constitution of the child and especially complicating diseases may prolong the attack many weeks. The season of the year when the illness sets in often influences the course, as it is shorter during the dry, warm months and longer during the winter months. The attack may be aborted by the early dose of vaccines.

COMPLICATIONS

These may be accounted for by the mechanical effects of the severe coughing and the lesions that may be caused by them directly and depend largely

on the intense venous congestion which accompanies the paroxysm. Hemorrhages of the mucous membranes of the nose, mouth, bronchi, etc., are all the effects of increased pressure. Epistaxis is the most frequent form, but is rarely severe enough to require local treatment. In young children bleeding from the mouth is often due to biting the tongue during a paroxysm. In hemorrhages into the conjunctivæ there is often a preceding conjunctivitis. Small hemorrhages into the cellular tissue around the eye sometimes give an appearance of an ordinary black eye. Multiple hemorrhages in the skin may occur and intracranial hemorrhages have been reported severe enough to produce death. They may result in paralysis, depending on the location and extent of the hemorrhage.

The most serious as well as the most frequent complications are those connected with the respiratory system. The most frequent cause of death is bronchopneumonia and is the most feared complication among young children. This generally begins as a bronchitis and extends rapidly until a capillary bronchitis with patches of consolidation result. The onset is apt to be insidious and the physical signs may be obscure in the early stages, but a rise in temperature is always to be looked upon with suspicion until the source can be explained. Young infants are especially susceptible to pulmonary complications, and few babies under six months of age escape. The physical signs of bronchopneumonia in whooping-cough present no peculiarities, although relapses are more common.

The emphysema which usually accompanies it causes an increase in the number of respirations out of proportion to the rise in temperature. Vesicular emphysema is present in most of the cases coming to autopsy. Cases have been reported of subcutaneous emphysema resulting from the rupture of air blebs which form on the surface of the lung, and the air finally is forced in the cellular tissue of the neck and even entire body. In such cases the skin crackles on pressure and produces a sensation like an air cushion.

Enlargement of the bronchial lymph-nodes in the mediastinum is found in a large proportion of the cases. The majority of these fortunately is a simple adenitis, although many of them become tuberculous and constitute a distinct menace to life. Whooping-cough may bring out a latent tuberculosis. Or they may develop after all the symptoms of whooping-cough have disappeared. The enlargement of these glands is responsible for the prolongation of the cough in many cases. The lungs may be the seat of active tuberculous processes. Quite a number of tuberculous children date their infection back to whooping-cough. This predisposition to tuberculosis which whooping-cough often leaves in its wake is one of the most serious results of whooping-cough.

On the part of the digestive system the commonest complication is that

of vomiting. This is a mechanical effect of the severe coughing. While it is a distressing symptom at any time, it is especially so in young infants as it seriously interferes with the nutrition of the child. The mere taking of food will start a paroxysm of coughing and this is accompanied with the vomiting. The impaired nutrition which follows makes the child an easier victim to pneumonia.

Diarrhea is a very frequent complication in infants, especially during the summer months. This may only be an occasional symptom, but it may become severe and prolonged and result in the development of ileocolitis. Ulcer of the frenum of the tongue is very frequent. This is a result of the protrusion of the tongue over the sharp edges of the lower incisors during a paroxysm of coughing.

Anorexia is a very frequent and disturbing complication. The children have no appetite and cannot be coaxed into eating. Forcing food sets up a paroxysm of coughing and does more harm than good. These children will not starve, but they lose in weight and their resistance to infection and other complications is diminished. After the disease has run its course children are very apt to develop an enormous appetite and seem to want to make up for the lost food.

Nervous System.—The most frequent among the complications of the nervous system are convulsions. They are more apt to occur in young infants, especially if they are rachitic. They are more common in severe attacks, but may occur in mild cases which have given no cause for anxiety. These convulsions are nearly always multiple, rarely appearing singly. They are especially to be dreaded if the child has bronchopneumonia. If the convulsion lasts steadily for over an hour an intracranial lesion should be suspected. This may be due to meningeal or cortical hemorrhages, encephalitis, hemorrhagic effusion or embolism. The symptoms appear under the usual types of cerebral paralysis, as monoplegias, hemiplegias, diplegias, etc. There may be disturbances of sight, speech and hearing.

Sudden blindness as a result of hemorrhages into the anterior chamber or retinal detachment is not infrequent in very severe cases. The visual power returns usually in a few days or weeks. The transient symptoms probably are the effect of circulatory changes that occur in the brain during the paroxysm, while those of longer duration may be the result of meningeal hemorrhage. Disturbances of hearing due to a complicating otitis media or a direct lesion of the central nervous system are not common.

Circulatory System.—Diseases of the heart, such as endocarditis, myocarditis or pericarditis are rare. Medical literature contains some references to damage of the heart from whooping-cough, and Ledbetter and White made a careful study of the literature and also of a series of hospital cases and found no evidence to show that whooping-cough has a damaging effect

on the heart. Cardiac failure does not appear to occur during the paroxysms of whooping-cough which may, however, produce a temporary mechanical strain, especially on the right side of the heart. Umbilical or inguinal hernia may in rare instances result from the sudden and greatly increased abdominal pressure during the paroxysms. These are uncommon complications.

Whooping-cough is often found associated with other acute infectious diseases. Measles are apt to occur after whooping-cough, as is chickenpox. This may be due to a lowered resistance as a result of the long strain during an attack of whooping-cough.

The Blood.—Increase of the white cells occurs in the early stages of the catarrhal stage. This leukocytosis is more marked in very young children and there may be three times as many white blood-corpuscles as in the normal condition. As a rule this leukocytosis is of the lymphatic variety and the lymphocytes may constitute 60 per cent of the total number of white cells.

Regan and Tolstonkov made an extensive study of the chemistry of the blood in whooping-cough and found there was a constant diminution of the total inorganic phosphorus associated with a lowering of the hydrogen ion concentration of the blood. These changes occur early in the course of the disease and suggest an acidosis of an uncompensated type. There is, as a result, the accumulation or increased concentration of free carbon dioxid in the blood. These laboratory findings, according to the authors, explain the prominent symptoms of whooping-cough, namely, paroxysms, vomiting, and convulsions. They found that alkalis administered early may abort the disease and shorten its course. In other words, if the acid base unbalance is corrected the clinical symptoms will be quickly ameliorated.

Urine.—A transient albuminuria is not uncommon in the catarrhal stage. It may be accompanied with a few hyalin casts. This is no doubt the result of circulatory changes in the kidneys. Acute nephritis is very rare. There is also a transient glycosuria in about 10 per cent of all cases, the explanation being that the glycogenic function is lowered in whooping-cough.

DIAGNOSIS

The diagnosis of whooping-cough is not always a simple matter, especially in the early stage. As this is the period of greatest contagion, an early diagnosis is necessary to prevent the spread of the disease. The paroxysmal stage in atypical cases renders no difficulties in the way of diagnosis. A very simple and often useful method of inducing a paroxysm of coughing is to press a finger firmly over the trachea in the suprasternal notch. If whooping-cough is present the child will immediately have a typical paroxysm ending in the whoop. Introducing a tongue depressor way back to the

pharynx will often start a paroxysm, as will tickling or irritating the nasal mucous membrane or the external auditory canal.

Neurath enumerates the positive data which can be taken into consideration for a diagnosis of whooping-cough. This was written before the positive identification of the Bordet-Gengou bacillus which if detected verifies the diagnosis in the very early stage.

1. Typical paroxysms of coughing after a period of catarrhal symptoms. The cough sets in with spasmodic expirations after a few intervening crowing inspirations (the whoop) terminating with the production of a tenacious glairy mucus.

2. The cough is more frequent at night. It may, however, be caused by hearing and seeing a paroxysm in another child.

3. The clinical examination reveals no signs in the lungs to account for the severe and violent coughing.

4. The great increase in the number of leukocytes.

5. History of exposure to infection, the same disease in members of the family and the existence of an epidemic.

6. Failure of medical treatment and the use of antispasmodics while the disease is on the ascent.

The bacteriologic diagnosis of whooping-cough is of great value. It is now generally admitted that the Bordet-Gengou bacillus is found in the largest numbers in the catarrhal stage. Young children swallow their sputum and it is difficult to obtain specimens. The method of using Petri dishes to catch the organism during a cough has been referred to before. This has been appropriately called the "cough-sowing" method. Meyer obtained positive cultures in 970 out of 1,106 cases. There were 75 per cent positive findings during the catarrhal stage, 57 per cent in the first week of the paroxysmal stage and only 9 per cent after the fourth week. When the bacteriological technic is improved no doubt simple diagnostic methods will be made available to the general practitioner, such as are now in use for the identification of the Klebs-Löffler bacillus in diphtheria.

Several recent observers report their belief that cases of whooping-cough are rarely positive culturally after four weeks and that the contagious stage of the disease is practically restricted to the catarrhal stage. A few years ago the French Minister of Public Instruction issued an order permitting children with whooping-cough to return to school after they had whooped a month.

The intradermal inoculation of pertussis vaccine has been recommended for diagnostic purposes. It is claimed that this offers a valuable means of early diagnosis.

Friedlander and Wagner made a careful investigation into the value of the complement fixation test in diagnosis. This method was employed by Bordet and Gengou and verified by many investigators. The summary and conclusions of Friedlander's study are:

1. The most reliable antigen for complement fixation tests in whooping-cough is obtained by autolyzing an aqueous emulsion of twenty-four to forty-eight hours' growth of the Bordet-Gengou bacillus for eighteen to twenty-hour hours at 56° F. and shaking for several hours.

2. An active serum may give non-specific reactions. A negative reaction given by active serum is stronger evidence of the lack of an infection than is a negative reaction by an inactive serum.

3. For fixation one-half hour in the water-bath or one hour in the incubator is absolutely reliable. Fixation at room temperature is unsatisfactory.

4. About 40 per cent of whooping-cough cases have given a positive reaction with antigens of the Bordet-Gengou bacillus when inactive serum was used. The highest percentage of positives is given by the convalescent vaccinated cases.

5. A $++$, $+++$, or $++++$ reaction by inactive serum with an antigen of Bordet-Gengou bacillus is diagnostic of whooping-cough. A $\pm$ or $+$ reaction is suspicious and a negative reaction has little significance.

They conclude that the complement fixation tests in serum from 111 cases of whooping-cough or suspected whooping-cough support the theory that the Bordet-Gengou bacillus is the etiological factor of the disease. The complement fixation test may be of value in the diagnosis of positive cases of pertussis. Very recently attempts have been made to diagnose whooping-cough in the early stages by means of the agglutination test. When the organism can be obtained in the first few weeks by the use of the Petri dish method or direct swabbing it is possible to make a diagnosis in the early catarrhal stage. A dilution of not less than 1 : 200 is necessary for a positive diagnosis by the agglutination test. Krumwiede and others found two serologic groups of the Bordet-Gengou bacillus by agglutination and agglutin absorption methods which they termed A and B. It is hoped that before many years this procedure can be simplified and made dependable, as it affords a means of making a positive diagnosis in the catarrhal stage.

While the cough ending with a whoop is characteristic, a similar cough with a similar ending may occur in other conditions. In certain cases of influenza there may be a cough identical to that of whooping-cough and the differentiation can only be made from examination of the blood and sputum

and the course of the disease. A similar cough can result from irritation of the pressure of enlarged tracheal or bronchial lymph-nodes on the pneumogastric or recurrent laryngeal nerves. A foreign body in the air passages may give rise to a spasmodic cough. The x-ray will help to clear up the diagnosis as will the course of the disease. In these conditions there is a prolonged duration of the cough and there are no distinct stages as in whooping-cough. Attacks of ordinary bronchitis in young infants not infrequently have more or less of a spasmodic character with a more or less typical whoop. A nervous or hysterical irritation cough may closely simulate the typical paroxysms of whooping-cough. Parents of nervous temperament may have this cough while their children are in the midst of the disease and whooping-cough may erroneously be diagnosed. In these cases the cough is not liable to occur at night. Reflex coughs from enlarged tonsils and adenoids may be difficult to distinguish at first from whooping-cough.

The examination of the blood is of great value in making a diagnosis in the catarrhal stage. The white blood-cells may be increased two or three times the normal, that is, from 20,000 to 30,000. The white cell-count reached 176,000 on the sixteenth day of whooping-cough in an eighteen-months-old infant. The lymphocytes are greatly increased at the expense of the polymorphonuclear neutrophils and may form 60 to 80 per cent of the total leukocytes. No other non-febrile affections of the respiratory tract show such an increase. Other possibilities for the leukocytosis must be searched for, such as pyelitis, infections, etc. The theory has been advanced that the white cells are forced into the blood stream mechanically by the force of the paroxysm.

The discovery of the specific organism has opened new channels of diagnosis. The Boston Commission for the Study of Whooping Cough advises the examination of cultures from suspected cases. The technic is simply to have the patient cough on to an open plate containing the medium and sending it to a laboratory for growth and examination similar to the common method of taking cultures in suspected cases of diphtheria. They claim that carriers, second cases and suspected cases without whooping may be recognized by this method. As the disease progresses there is a corresponding decline in the percentage of positive cultures. They suggest that the existing quarantine methods be changed so that the quarantine is lifted only by release cultures as is done in diphtheria.

PROGNOSIS

This is a disease which kills over twenty-five thousand children each year in the United States. In the first two years of life it is more fatal than any of the communicable diseases of childhood. It is a serious and dangerous

disease in young infants. The age of the child is the most important factor in the prognosis of whooping-cough. Nearly two-thirds of the deaths from whooping-cough occur in the first year of life. This is the result of the complications of bronchopneumonia, digestive disturbances and convulsions which are particularly fatal conditions in young infants. Few infants with a complication of bronchopneumonia survive. The environment, season and social status of the parents are all concerned in the prognosis. Among the poor, especially in the crowded sections of our cities, and in institutions, such as foundling and orphan asylums, the mortality is high. Overcrowding, insufficient air, improper hygiene, poor food and unintelligent care are important factors in course and termination of the disease. The preceding physical condition of the child has an important bearing on the prognosis. The prognosis is better in summer than in winter because the child can be out of doors and have plenty of fresh air, and bronchopneumonia is less frequent in the summer months. The prognosis is bad in children who have a latent tuberculosis or a predisposition to it. Whooping-cough is a frequent predisposing cause of generalized tuberculosis. It is not so good in children subject to bronchitis or asthma or who have active rickets. The number of paroxysms may be an index of the severity of the disease. According to Rousseau over sixty attacks a day constitute a bad prognosis. Long intervals free from attacks with good physical condition are the signs of a favorable normal course of the disease.

The accompanying tables, compiled from the statistics of the New York State Department of Health, are of interest in comparing the morbidity and mortality month by month for eleven years. There seems to be no uniformity in the seasonal prevalence, although there are fewer cases in the summer months. Here the children are out of doors and do not come in as close contact as in the winter months when they are in school. It is difficult to explain why the percentage of deaths in the summer months is so high. There is practically no difference in the mortality rate between the cities

TABLE XII.—MORBIDITY FROM WHOOPING-COUGH PER 100,000 POPULATION IN NEW YORK STATE, 1915 TO 1925, ACCORDING TO MONTHS

Year	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1915.....	106.5	133.0	130.8	126.2	128.4	145.8	166.5	151.2	111.4	127.2	138.1	149.0
1916.....	167.1	166.3	212.0	230.1	264.0	249.0	265.3	199.0	92.0	68.5	82.9	74.9
1917.....	92.8	121.5	120.6	174.2	193.7	201.3	271.6	237.6	168.2	184.0	216.4	189.3
1918.....	263.9	235.8	243.5	240.0	235.8	196.0	175.3	125.7	90.6	49.7	48.9	38.2
1919.....	30.8	38.6	31.6	25.9	43.1	46.1	86.0	76.3	69.4	93.4	146.9	153.8
1920.....	222.3	196.5	246.3	181.7	183.0	210.7	234.4	215.3	167.8	132.6	198.7	244.9
1921.....	271.6	340.1	280.9	268.5	247.4	233.7	201.0	152.0	108.7	75.9	80.8	113.4
1922.....	109.2	137.0	132.1	128.1	130.9	150.7	132.0	139.7	129.9	133.2	156.7	157.2
1923.....	203.9	188.4	184.3	192.6	163.9	138.5	133.6	122.2	109.0	111.7	150.9	183.6
1924.....	236.2	229.8	223.4	223.0	211.5	206.2	231.4	192.3	172.6	147.4	124.6	154.2
1925.....	154.1	162.5	163.0	173.6	145.8	140.2	145.6	110.5	94.1	94.3	99.4	133.2

TABLE XIII.—MORTALITY FROM WHOOPING-COUGH PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1925, ACCORDING TO MONTHS

Year	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1915.....	5.1	7.8	8.1	9.5	8.2	7.4	7.6	10.5	9.0	5.0	7.1	6.9
1916.....	8.3	8.1	8.0	9.3	10.1	10.1	9.1	12.0	6.5	2.7	2.8	2.4
1917.....	3.5	5.7	5.1	6.1	5.7	6.7	9.3	16.3	17.9	9.4	10.2	9.9
1918.....	12.5	14.4	20.3	20.8	14.6	10.8	9.7	9.9	7.4	15.9	5.8	3.9
1919.....	2.8	2.0	2.1	2.7	1.6	1.6	4.6	3.5	3.4	2.7	2.2	4.4
1920.....	6.9	18.0	12.9	9.8	8.4	9.2	10.3	11.9	11.8	6.0	4.0	7.0
1921.....	6.7	11.3	10.9	10.3	9.0	6.0	8.9	7.2	6.3	3.7	3.0	2.7
1922.....	2.7	6.6	6.1	7.0	4.4	3.2	4.3	4.2	5.0	3.7	2.9	2.8
1923.....	3.5	7.1	7.6	5.7	3.8	5.3	5.1	4.3	4.5	2.7	3.8	3.5
1924.....	5.7	5.8	7.3	6.3	7.0	7.1	7.4	6.1	7.9	3.5	4.8	4.6
1925.....	2.5	5.8	5.3	6.3	5.3	4.6	4.4	5.2	2.9	3.6	2.3	3.6

TABLE XIV.—MORTALITY FROM WHOOPING-COUGH PER 100,000 POPULATION OF THE UNITED STATES DEATH REGISTRATION AREA OF NEW YORK STATE FROM 1915 TO 1925

Year	United States Registration Area	New York State	New York City	New York State Exclusive of New York City
1915	8.1	7.7	7.6	7.7
1916	10.2	7.4	6.6	8.4
1917	10.5	8.8	9.1	8.6
1918	16.9	12.2	12.1	12.2
1919	5.5	2.8	2.9	2.8
1920	12.5	9.6	10.9	8.1
1921	9.1	7.1	6.2	8.3
1922	5.6	4.4	4.7	4.1
1923	9.7	4.7	3.5	6.1
1924		6.1	6.6	5.7
1925		4.3	5.2	3.3

TABLE XV.—DEATH RATE FROM WHOOPING-COUGH PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1924, ACCORDING TO AGE

Age, Years	Number		Rate		Per Cent of All Cases	
	1915	1924	1915	1924	1915	1924
Under 1.............	432	386	177.8	165.1	1.8	2.4
1	197	179	105.8	83.7	3.7	5.8
2	58	49	29.3	22.3	2.8	3.3
3	25	26	12.8	11.8	1.9	2.8
4	10	14	5.3	6.5	1.1	1.8
5-9	28	17	3.1	1.6	1.0	.7
10-14	1	...	.1	...	.1	..
15 and over	9	5	.1	.1	.01	..
TOTAL ALL AGES.	760	676	7.7	6.1	.5	.5

and the country districts. The age incidence as seen in Table XV demonstrates the very high mortality in young children. There are practically no deaths in children over ten years of age.

PROPHYLAXIS

Prevention is of the utmost importance where young infants are concerned as well as delicate children and children who have a predisposition to tuberculosis. Unnecessary exposure is never justifiable. It is a mistaken idea that a child might as well contract whooping-cough at one time as another. The younger the child the more serious is the disease, and the longer it is avoided the greater is the ease of recovery. It is very difficult to control whooping-cough, as many cases in the early stages are never diagnosed and never are under medical supervision. There are many cases so mild that they are unrecognized. The only chance of preventing the spread to others in the early and most contagious stage depends upon a thoughtful and intelligent mother who isolates her child if he suffers from a cold. If parents would observe the Golden Rule when their children contract whooping-cough its spread would be greatly curtailed. This means that a child with suspected whooping-cough should be kept away from school, Sunday school, moving picture shows or any place of public assemblage. He should not be allowed on the street unless accompanied by a responsible person who is able to keep the child from contact with children who have not had the disease.

A physician is required by law to report promptly to the local health officer all cases of whooping-cough which he is called upon to treat. Later on when the case has fully recovered he should so inform the health officer. When a case is discovered in school the child should be at once excluded from school and the health authorities notified by either the school physician or nurse. In this way the younger children at home can be sent to some other home unoccupied by children or kept away from the infected child.

The quarantine period is from six to eight weeks, although the time limit varies in different cities. The quarantine should not be raised until at least three weeks after the whoop develops. The method used by the Health Department of Chicago is excellent. They quarantine the child in the house or yard for the first two weeks, then allow him the freedom of the streets the next three weeks, provided the child is with an attendant and wears around the arm a yellow band bearing the words "whooping-cough" in black letters.

As the disease may possibly be carried by a third person, all persons coming in contact with the affected child should observe due caution. This applies to nurses and physicians as well as members of the family.

The prophylactic use of pertussis vaccine warrants its use in every case of exposure, especially of young children and in children's institutions. The vaccine is employed both as a prophylactic and a therapeutic agent and its use will be referred to under specific treatment.

Herrman recommends hospital care of young children with whooping-cough. This can be easily accomplished in institutions and it lessens the chances of the epidemic spreading, for the children are under strict control as long as the disease is contagious.

It is not necessary to disinfect or fumigate the rooms occupied by the child, as is done in some of the other diseases. A careful general cleansing is sufficient.

TREATMENT

Probably in no other disease have there been so many sure cures and superstitions as in whooping-cough. There must have been at least nine hundred and ninety-nine positive "remedies," which means that we have no sure cure. While most of these remedies have little or no influence on the course of the disease, yet their administration is a great comfort to the parents and have therefore some value.

The general management is important and this includes general hygienic measures which tend to improve the health and condition of the child. Most of the cases in older children require nothing more.

Fresh air is an important aid in the treatment. It is a well-recognized fact that fewer paroxysms occur in the daytime when the children are out of doors than at night or when they are indoors. Fresh air treatment where all chance of chilling is avoided usually brings about an improvement. Older children with whooping-cough may go out in all seasons, except on stormy or windy days. Young and delicate infants should be more carefully protected, but should be given all the fresh air—both day and night—possible. The two-room system should be employed in such cases, one of which is thoroughly aired while the sick child remains in the other. The much-vaunted change of air is of value only if it is equivalent to an improvement of the climatic conditions. During the summer months a warm place at the seashore is beneficial and a sea voyage is of great help. Here we have a dust free, fresh atmosphere. Fresh air is not a synonym for cold air, and the child's room should have plenty of fresh air with a temperature of 65° to 70° F. The rooms should be frequently changed, aired and cleaned. The clothing should be warm but not heavy or in excess. They should be clothed for indoors and when they go out of doors necessary extra wraps or a sweater should be put on and removed when returning to the house. Cotton knitted underwear is better than woolen as it absorbs the perspiration more readily and can be sterilized by boiling without shrinking or injuring the garment. The bed-

ding at night during winter should be warmed, as cold sheets are apt to bring
on paroxysms of coughing when the child comes in contact with them. The
clothes should be fastened so that suspenders, strings, bands or binders do
not interfere with the respiratory function and the mechanism of coughing.
There is no objection to a daily bath and sponge bath at night, provided
precautions are taken to avoid exposure. Herrman strongly recommends
keeping children with whooping-cough in bed. The bed should be kept in
the open air during the daytime. Children treated this way do not have so
many paroxysms and do not suffer from digestive troubles and are less likely
to lose weight. When the child is in bed there is less stimulation of the
nervous system. The diet should be light but nutritious. It necessarily
varies with each individual case and taste. In young infants the chance of
recovery is increased if fortunate enough to be breast-fed. The milk formula
must be adapted to the digestive needs of the infant. When there is much
vomiting the use of thick cereal gruels is of advantage, as they are often
retained when a fluid milk is vomited. The feeding is similar to that em-
ployed in pylorospasm. A milk diet is often well borne in older children
when the vomiting is severe. Small quantities of food given at frequent
intervals are retained better than three large meals a day, for copious meals
are apt to excite coughing, and this may account for the distaste for food.
When a meal is lost after an attack of coughing another can be given at once.
The best time to administer food is after a paroxysm. Regulation of the
diet is an important therapeutic measure, as it is so closely concerned with
nutrition.

A daily movement of the bowels should be obtained and this can be
accomplished by simple remedies such as mineral oil, milk of magnesia or
aromatic cascara. The use of laxatives or low enemata will prevent disten-
tion of the bowels. Abdominal distention may increase the frequency of the
paroxysms and should be avoided. In some children milk will cause disten-
tion, and when it is discontinued the distention disappears. Any medication
that causes disturbance of the stomach or intestine should be discontinued.

Local applications in the nose, pharynx or larynx by means of swabs or
sprays were widely used many years ago. They are not in general favor at
the present time. They should never be used for small children. Solutions
of resorcin 3 per cent, quinin 10 per cent or bichlorid 1 per cent have been
recommended. Cocain should never be locally applied for children. In-
sufflations of orthoform, boric acid and quinin in the nasopharynx and larynx
find favor in the hands of some physicians. Inhalations are of much more
value. They relieve the spasm, modify the catarrhal symptoms, allay the
bronchitis and facilitate the expulsion of the mucus. They are said to
diminish the number and the severity of the paroxysms. They possibly have
some use as antiseptics. Among the drugs used in this manner may be

mentioned creosote, formalin, 1 per cent solution of carbolic acid, oil of turpentine, benzol, etc. These substances can be used on cotton in a respirator or steam atomizer, or vaporized over an alcohol lamp. Steam medicated with the oil of eucalyptus or compound tincture of benzoin is of value, especially in cases complicated by bronchitis or bronchopneumonia. Chloroform should be used for convulsions or when the paroxysms are frequent and of great severity. In cases in which asphyxia occurs, intubation, such as is used in diphtheria may be employed with distinct benefit. There are several proprietary remedies used externally as inunctions or in the form of plasters which are of very doubtful efficiency. The rectal administration of quinin has proved of value in the treatment of some cases of whooping-cough.

Internal Medication.—All sort and kinds of medicines have been recommended. This natural mode of administration is more popular and more successful than local applications. Any remedy seems to have a transitory success and leads to a frequent change of prescription, but it is doubtful if any of the internal remedies lead to any safe, sure and lasting benefit. Holt stated that in his experience of the innumerable drugs which have been recommended for this disease there are only two which possess undoubted advantages over all the others, namely, belladonna and antipyrin. Belladonna should be started with a small dose and cautiously increased. It is surprising how tolerant young children are of this drug. For an infant one year of age the first dose should be ⅙ minim of the fluid extract every four hours. The interval is then increased to two hours and then the dose to ¼ grain. If atropin is used, one drop of a 1 : 1,000 solution is given every two hours, increasing to two or even three drops. The belladonna can be given until the physiological signs appear, such as dilation of the pupils and flushing of the skin. Antipyrin is a safer and more satisfactory remedy. Young infants can take relatively large doses with safety. For example, an infant a year old can take 2 grains every two or three hours. Bromid of soda can be combined with the antipyrin and it increases its antispasmodic effect. The following prescription is recommended:

℞   Antipyr. ....ʒi
        Sod. Brom. ....ʒss
        Glycerin. ....ʒii
        Aq. Anisi q.s. ....ʒiv

One-half teaspoon in a little water every two or three hours.

Luminal in the powder form or as an elixir benefits some children. A year-old infant can take ¼ grain every three hours. Quinin is an old-fashioned remedy which is still a favorite with many physicians, and is used very generally in Germany. One grain of the sulphate of quinin can be given to a child one year of age every three hours. It is a disagreeable drug to admin-

ister, but there are a number of derivatives which are easier to take. Quinin preparations are best given in full doses for three days, then in half doses for six days and then discontinued for a few days. The quinin can be combined with belladonna.

If the paroxysms are so severe at night as to disturb sleep it may be advisable to use small doses of opiates, such as codein, paregoric, chloral, allonal, amytal or trional. Too long or indiscriminate use of these drugs should be avoided. While it is doubtful if any drug shortens the length of the disease, they will reduce the number and severity of the paroxysms and have therefore decided value. It is a wise plan to use the antipyrin and bromid of soda for a week, then try belladonna or quinin the next week. In a mild case with not more than ten paroxysms a day and where there is no vomiting and no impairment of the general health there is no use in giving any drug except a single dose of codein or antipyrin at bedtime.

Benzyl benzoate is a new antispasmodic drug which has proved helpful in the hands of some physicians. It is used in a 20 per cent solution and the only objection to its use is its unpleasant taste.

Intramuscular injections of ether first came into popularity in the treatment of whooping-cough about five years ago and its benefits have been attested to by a great many clinicians. Pollock of New Orleans treated 107 cases ranging in age from two months to nine years by this method. In eight of these pneumonia had set in before the treatment and one after the injections. The other injections were given to all cases, including those with pneumonia. The dose was from ½ to 2 c.c., depending on the weight, age and severity of the attack. The injections are made deep into the muscle of the buttocks behind the middle of a vertical line drawn from the great trochanter to the crest of the ileum. The sulphuric ether used ordinarily for anesthesia is used and is taken directly from the can and injected deep into the gluteal region. These injections do not cause any more pain than the injection of vaccine. The pain, which is burning in character, disappears in a couple of minutes. The odor of ether can be detected in the breath within thirty minutes of the injection and this lasts from four to six hours. These injections are given every other day for six to eight doses. Tow of New York who employed this treatment reports that fifty out of sixty-one children treated, or 82 per cent, were decidedly benefited in that the number of paroxysms were reduced and their severity lessened, they slept better, the appetite improved and there was not so much vomiting. Eleven of his cases or 8 per cent were not aided. The effect of the ether is due to its antiseptic and antitoxic effect as well as its antispasmodic and narcotic properties.

From the successful experience of so many physicians in this country and in Europe it would seem that this mode of treatment deserves wider

use. The earlier the treatment is commenced the more likely is the possibility of a successful result.

The use of the x-ray has been recommended and it can with safety be used in conjunction with other modes of treatment. The claims of its enthusiastic introducers have not been entirely corroborated and the treatment is still in the experimental stage. It seems that the lymphocytosis disappears after one or two exposures and the action of the x-ray on the bronchial lymph-nodes. The treatment is usually one to three exposures at two to three day intervals with a tube distance of 28 or 14 inches. The dosage is 4 milliamperes with 2 milligram aluminum filter and 7 inch spark gap.

Quite recently the use of ultraviolet rays has been employed with some success in the treatment of whooping-cough. This is done by exposing the chest, back and front, for five minutes every two or three days and regulated according to the skin reaction. The paroxysms are reduced in severity and number, but the duration of the disease as a whole is not shortened. Concentrated ultraviolet rays either from the sun or Kromayer lamp direct in the pharynx have been used with benefit in some cases.

Specific Vaccine Treatment.—There is no question but that the greatest and most promising advance in the treatment of whooping-cough has been in the use of vaccines both as a curative and a preventive measure. This treatment was made possible by the discovery of the specific organism of whooping-cough—the Bordet-Gengou bacillus. Much work has been and is being done along these lines, and while the vaccines do not cure all cases at once they undoubtedly do shorten the paroxysmal stage and diminish the severity and frequency of the attacks. The vaccines prepared from the pure culture of the Bordet-Gengou bacillus are to be preferred to the mixed vaccines. Undoubtedly there are several strains or types of Bordet-Gengou bacilli, so the vaccine should be polyvalent in the sense of containing the different types. The mixed vaccines prepared by some of the biological laboratories contain besides the Bordet-Gengou bacilli, *Micrococcus catarrhalis, Staphylococcus aureus, Staphylococcus pyogenes, Bacillus influenzæ,* and some have in addition the four types of pneumococci. A veritable shotgun mixture. The weight of evidence after fifteen years of investigation is that the reaction following the use of the Bordet-Gengou vaccine is specific and that there is no advantage in the mixed vaccines, nor is it essential that it must be freshly prepared as advised by some authors in order to obtain the best results. Park, as a result of experimental work on animals, came to the conclusion that as far as antibody response was concerned there is no appreciable difference between freshly prepared vaccines and that stored for a few months. When whooping-cough breaks out in an orphan asylum or institution for infants it would be advisable to pre-

pare an autogenous vaccine from the first cases to be used for immunizing and treating the other children.

Prophylaxis.—There is very positive evidence that this vaccine will immunize children against this disease, and when a child has been definitely exposed, is the only means of prevention. The writer reported in 1916 the results of the use of vaccines prepared from pure cultures of the Bordet-Gengou bacillus in an institution for infants. In four different epidemics of whooping-cough 164 children were exposed and only 7 per cent of these children contracted the disease. Before the vaccines were used it was found impracticable to quarantine each case, and over 60 per cent of the children came down with whooping-cough. These results have been confirmed by different clinicians both in this country and abroad. Similar results have been obtained in private practice, and it is most likely, if the vaccines are injected promptly and in sufficient dose, to prevent the occurrence of the disease in a child or children who have been definitely exposed in school or from other children in the family or neighborhood. The vaccine is injected with a sterile hypodermic needle and syringe subcutaneously. The site of injection should be cleansed with soap and water and disinfected with alcohol or with tincture of iodin applied to the dry surface. For prophylactic use three injections should be given two to three days apart. The dosage now given is larger than was formerly advised. For a year-old infant it is best to use two thousand million the first dose, four thousand million the second and six thousand million for the third dose. No severe reactions result from giving these large doses, although a small percentage of cases may have sore arms for a few hours. Febrile reactions are very rare.

Therapeutic Injections.—The same technic is used as mentioned above in regard to prophylactic injections, and the same dosage should be given. Four to six injections should be administered, the last two being eight thousand million and sixteen thousand million. The earlier in the course of the disease the vaccines are given the greater improvement will be noticed and the number and severity of the attacks will be reduced and the duration of the disease shortened.

Complications.—The treatment of complications requires no special discussion. Bronchopneumonia is treated according to approved modern methods. The use of the vaccines or the injection of ether would not interfere with the usual treatment. Plenty of fresh—not cold—air is indicated and it may be advisable to control the cough with opiates. The heart should be stimulated and small doses of strophanthus are less liable to upset the stomach in young children than digitalis. A tight abdominal binder gives great relief in controlling vomiting in whooping-cough. Special belts for this purpose are on the market, or a wide stockinette bandage may be wrapped around the abdomen tightly from the pelvis to the sternum.

PUBLIC HEALTH REGULATIONS

Whooping-cough is a reportable disease and every case must be reported promptly to the local health officer. No quarantine is required in New York State but a child having the disease is not permitted to attend any private, public or Sunday school or any public or private gathering for at least eight weeks after the development of the disease or until one week after the last characteristic cough. Regulations differ in various city and state departments of health. Ohio, for example, prescribes isolation of the patient for a period of at least two weeks from the development of the characteristic cough. The patient is permitted "to go into the streets when under the observation of a responsible person, providing he wears in plain view on the upper left arm a band on which there shall be printed the words 'Whooping Cough' in letters not less than one inch in height."

The school authorities in New York State exclude all children suffering from whooping-cough for eight weeks from the onset or until one week after the last characteristic cough. Other children of the same household who have never had the disease are excluded until the termination of quarantine and fourteen days from the date of complete isolation of the patient. This period is extended if a cough develops. Children who have had whooping-cough are permitted to attend school even though exposed at home. If the other children in the same household are sent away when the disease is discovered and have never had whooping-cough, they are excluded from school for two weeks after the removal or longer if a cold or cough develops.

The résumé of the principal features of whooping-cough as given by the Committee on Control of Communicable Diseases by the American Public Health Association is as follows:

1. INFECTIOUS AGENT.—Pertussis bacillus of Bordet and Gengou, *Hemophilus pertussis*.

2. SOURCE OF INFECTION.—Discharges from the laryngeal and bronchial mucous membranes of infected persons (rarely also of infected dogs and cats, which are known to be susceptible).

3. MODE OF TRANSMISSION.—Contact with an infected person or animal or with articles freshly soiled with the discharges of such persons or animals.

4. INCUBATION PERIOD.—Commonly seven days, almost uniformly within ten days.

5. PERIOD OF COMMUNICABILITY.—Particularly communicable in the early catarrhal stages before the characteristic whoop makes a clinical diagnosis possible. The catarrhal stage occupies from seven to fourteen days. After the characteristic whoop has appeared the communicable period continues certainly for three weeks. Even if the spasmodic cough with whoop persists longer than this it is most unlikely that the infecting organism can be isolated from the discharges. The communicable stage must be considered to extend from seven

days after exposure to an infected individual to three weeks after the development of the characteristic whoop.

6. METHOD OF CONTROL

(a) The infected individual and his environment

1. *Recognition of the Disease.*—Clinical symptoms, supported by a differential leukocyte count, and confirmed where possible by bacteriological examination of bronchial secretions. A positive diagnosis may be made by bacteriological examination of laryngeal discharges as early as one week before the development of the characteristic whoop.

2. *Isolation.*—Separation of the patient from susceptible children, and exclusion of the patient from school and public places for the period of presumed infectivity.

3. *Immunization.*—Use of prophylactic vaccination recommended by some observers. Not effective in all cases.

4. *Quarantine.*—Limited to the exclusion of nonimmune children from school and public gatherings for ten days after their last exposure to a recognized case.

5. *Concurrent Disinfection.*—Discharges from the nose and throat of the patient and articles soiled with such discharges.

6. *Terminal Disinfection.*—Cleaning of the premises used by the patient.

(b) General measures

Education in habits of personal cleanliness and in the dangers of association or contact with those showing catarrhal symptoms with cough.

CHAPTER IX

MUMPS

Definition.—Mumps is a specific communicable disease characterized by swelling and tenderness of one or more of the salivary glands, usually the parotids, accompanied with fever and mild constitutional symptoms.

Synonyms.—Parotitis epidemica; Ziegenpeter, Bauerwetzel; les oreillons; orecchioni, stranguglioni.

History.—This disease was recognized and described by medical writers of antiquity. A classical description appears in the writings of Hippocrates who lived in Greece from 460 to 370 B.C. In describing an epidemic he had observed in Thasos he wrote: "Ardent fevers occurred in a few instances, and these very mild, being rarely attended with hemorrhage, and never proving fatal. Swellings appeared about the ears, in many on either side, and in the greatest number on both sides, being unaccompanied by fever so as not to confine the patient to bed; in all cases they disappeared without giving trouble, neither did any of them come to suppuration as is common in swellings from other causes. They were of a lax, large, diffuse character, without inflammation or pain, and they went away without any critical sign. They seized children, adults and mostly those who were engaged in the exercises of the palestra and gymnasium, but seldom attacked women. Many had dry coughs without expectoration and accompanied with hoarseness of voice. In some instances earlier, and in others later, inflammations with pain seized sometimes one of the testicles, sometimes both; some of these were accompanied with fever and some not; the greater part were attended with much suffering. In other respects they were free of disease so as not to require medical assistance" (Ruhräh, *Pediatrics of the Past*).

So through the ages description of mumps appears in many medical writings. The contagious nature was recognized by the Arabian physician Rhazes. Chalmers of Charleston, South Carolina, in 1744 was the first to describe an epidemic of mumps in this country. Many humorous references to this disease appear in the literature of past ages showing that the laity has long recognized the benign nature of mumps.

Etiology.—This disease is not confined to any one race or climate of the world. Epidemics have been observed on every continent on this globe. It appears to be more prevalent during the winter months in this temperate

climate. This may be explained on the ground that houses are better ven-
tilated in summer than in winter. It occurs most frequently in children be-
tween the ages of five and twelve, the time when they are grouped together
in school. It is rare in very young children, although cases have been
reported in babies three weeks and seven months of age. At the other
extreme of life this disease has occurred in a woman of eighty-four and
a man ninety-nine years old. Epidemics are more common where young
people come into close contact, as in school, college or in military service.
Epidemics are particularly frequent in institutions, prisons, etc., where large
numbers of young persons are crowded together. During the World War
soldiers coming from rural districts who had never had mumps contracted
the disease in camp. There were nearly two hundred thousand cases treated
in the various camps in the year 1918. In spite of the frequency among the
soldiers in camp yet there is no special predisposition on the part of males.
It occurs as frequently in girls' schools as in the boys.

The epidemics spread slowly and can be limited to one group of indi-
viduals, provided they are kept from mingling with others. This can be
accomplished in a school or institution. It was impossible to control in the
army, as the troops were continually on the move. In a city an outbreak
may continue for several years with cases developing from time to time.
It may be associated with other contagious diseases.

Transmission.—This disease is spread by direct contact and transmit-
ted from person to person probably through the saliva. There is a possibility
of indirect transmission where a third person may spread the contagion if
his hands or clothing have been contaminated with the virus. There has
been no proof of the existence of healthy mumps carriers, although this may
be possible. Transmission by fomites or inanimate objects is rare, although
cases have been reported where such a condition seemed to explain an out-
break of the disease, as for example a person contracting the disease after
sleeping in a bed that had previously been occupied by a patient with mumps.
It is not known how long the mumps virus can remain active in the saliva
after it has left the body or how long it can resist drying. There is no
evidence to show that it can be transmitted by means of milk, water or food.

The disease may be contracted from a person before the development of
any symptoms. One of my patients, a young school girl, went to spend her
Christmas vacation in Boston and three days after her return home received
word that a child in the family in which she was visiting came down with
mumps two days after her departure. The girl was sent to school and
careful watch was kept to observe any signs of illness or swelling, which
developed about three weeks later. Three weeks after this several cases
developed among her classmates and mumps was not stamped out of the
school for several months. The period of infectiveness which begins several

days before the onset of the parotid swelling continues while the swelling lasts. Some instances have been reported where it was contagious for six weeks after the attack. As we have no method or means to determine whether a patient is capable of transmitting the disease, it would seem safe to quarantine for at least two weeks after the swelling has disappeared. This is not difficult to control with young children when the parents coöperate. The susceptibility is not so great as in measles and only from 25 to 50 per cent of children who are exposed will contract the disease. Barthez and Sauné reported an outbreak in a boys' school where 540 were exposed and 230 came down with the disease. One attack appears to insure immunity from future attacks. Occasional second attacks have been recorded and among the 230 cases observed by Barthez and Sauné there was a history of a previous attack in thirty cases.

Hess injected serum obtained from patients who had recovered from mumps in twenty children who were exposed to the disease and none of them contracted it. While this is a very small number of cases, yet it proves that the blood contains immunizing properties.

Bacteriology.—A number of organisms have been investigated in hunting for the specific organism of mumps. The earlier workers attempted to isolate ordinary non-filtrable bacteria. They were sought in the saliva, blood and parotid glands. The most complete study at that time was made by Laveran and Catrin in 1893. They isolated an organism in pure culture from the saliva, the blood, the testicle and puncture of the swollen parotid glands. This was a Gram-negative micrococcus occurring in pairs. Attempts to reproduce the disease by inoculation in animals were unsuccessful. A number of other observers found different organisms, but were not able to inoculate or infect animals so they developed symptoms of mumps.

Granata in 1908 approached the subject from a different angle and obtained saliva from patients with mumps and passed it through a filter and inoculated it into rabbits by injections into the blood, parotid glands and subcutaneous tissues. This proved successful. Further studies with this filtrable virus have been made by Martha Wollstein on cats as they are quite susceptible to mumps. She used mouth washings of patients suffering from mumps which were filtered through a Berkefeld filter. It was found that the virus was detected most readily in the saliva during the first three days of the disease and never after the ninth. Its presence was also detected in the blood. It was also demonstrated that the serum of cats who had recovered from the disease when injected into normal cats prevented them from developing the disease from inoculations of the virus. These observations of Wollstein prove that mumps is caused by a filtrable virus which can be obtained from the saliva and blood of patients with the disease and

this virus can reproduce the symptoms when injected in the parotid gland of cats and monkeys. Domestic animals sometimes catch the disease by close contact with persons suffering from it. A young man in my practice came down with mumps and his dog developed parotitis exactly eighteen days after exposure.

Pathology.—The parotid gland is the one most frequently affected and it becomes greatly enlarged and of a deep pink color which is a decided contrast to the pale yellow of the normal gland. According to Virchow the inflammation is confined to the intra-acinous and periacinous tissue, while the glandular canals and epithelium remain normal.

The most recent and valuable contribution to the pathology of this disease is by Martha Wollstein. Her work was on inoculated or experimental cases. The inoculated gland was found moister than the uninoculated gland and on section showed a gray cloudy appearance from the swelling of the acini. This was found in either the inoculated parotid, submaxillary or sublingual glands. These areas of cellular infiltration are always multiple but are more pronounced in some parts of the gland than in others. The adjacent lymph-nodes were usually congested but not enlarged. The infiltration was most intense about the secretory ducts which were sometimes dilated and the epithelium swollen and clouded. This is shown at the opening of Steno's duct which projects a short distance beyond the surface of the mucous membrane. Cowie described this appearance as characteristic of the disease. The orifice of the duct is pale and edematous, while there is a bright red central spot. Minute hemorrhagic points are often seen surrounding the duct.

The same microscopic changes were found in the testicle which may be greatly enlarged.

Symptoms.—*Period of Incubation.*—There is considerable difference of opinion among authorities regarding the length of incubation. It is usually long and the average is from eighteen to twenty-one days. Variations are recorded in from three to twenty-five cases. The Commission of the Clinical Society of London made a study of this disease in 1892 and placed the average incubation period at twenty-one days. There appears in the literature undoubted cases of mumps developing five weeks after exposure. There is a possibility of a second exposure in these cases of apparent long exposure.

One attack usually gives immunity and second attacks are rare, although they do occasionally occur.

Onset.—Slight prodromal symptoms are often present although their significance is not realized until after the gland becomes swollen. There may be slight indisposition and malaise several days before the swelling. The child becomes cross and cranky and loses his appetite and does not care to

play. It has been shown that the disease is contagious before the characteristic enlargement of the parotid.

In most cases the first and striking symptom is the swelling in the region of the parotid gland. This is usually accompanied by fever which may be preceded with a chill. The child feels sick and vertigo is a distressing symptom in some cases, while in others there are vomiting and diarrhea. Nosebleed occurs in some cases. The appetite goes and older children often complain of headache. There may be severe nervous symptoms with symptoms of meningeal irritation.

The Salivary Glands.—The parotids are involved in the great majority of cases. The parotids may be free and only the submaxillary affected. Cases in which only the sublingual gland was swollen have been reported. All three glands may be affected at the same time, although this is rare.

When the parotid is affected one or both sides may be involved. The left gland is more often affected at first than the right. Sometimes both glands are swollen at the same time. When it starts in one gland it usually spreads to the other in two to seven days. The swelling increases rapidly and its extent varies in different patients. It remains stationary for two or three days and then gradually subsides so that the gland appears normal after a week or ten days, but it may be palpable for three weeks or longer. The swellings disfigure the face of the child. The size of the swelling is subject to great fluctuations and it may be so large as to make the child unrecognizable. It usually gives the child a grotesque appearance. The swelling causes inconvenience in opening the mouth and in eating and chewing. In mild cases there is no sensitiveness on pressure, but where the swelling is intense it may be very painful. The swollen parotid gland is seen along the ramus of the jaw in front of the auricle of the ear. It extends over the cheeks, and the lobule of the ear which the swelling pushes out is in the center of the swelling. This position of the lobule of the ear is pathognomonic of a swollen parotid. In enlargement of the parotid gland the small fossa just below the ear and behind the angle of the jaw is obliterated. This is an important diagnostic point. The swelling may exceed these boundaries and spread upwards and downwards. The swelling of the submaxillary or lingual glands extends down the neck as far as the clavicle and may entirely obliterate the normal curve of the neck.

The swelling feels rather boggy at the onset, but later becomes firm and tense. There may be a decided erythema over the surface. The skin is tense and shiny. The gland itself feels doughy or tensely elastic.

Pharynx.—Very often there is a slight redness of the pharynx and in severe cases the uvula and tonsils may be edematous and cause considerable difficulty in swallowing. The buccal mucous membrane may be slightly congested at the onset, but the distinctive feature is the orifice of Steno's

duct on the affected side which is edematous and slightly protruding with a reddened orifice and often surrounded by a ring of deeper redness. If the swelling is great it may press the tonsils inwards and interfere with swallowing. There have been fatal cases of edema of the larynx.

Saliva.—The saliva is normal in composition. That is, there is no change in its digestive ferments. It may be normal in quantity or secreted in great excess or may be greatly diminished. When the saliva is diminished the mouth is dry and mastication is difficult. On the other hand, if secreted in large amounts it tends to collect in the mouth and overflow, especially if swallowing is painful. The lymph-nodes which drain the parotid and maxillary glands may be enlarged, showing the virus enters the lymphatic system and from there to the blood stream. Many cells are seen in the saliva such as lymphocytes and polynuclears, and in later stages of the disease epithelium and casts are present. When the swelling subsides these cellular elements disappear and the saliva returns to normal.

General Symptoms.—Fever is present in most of the cases, but there is no characteristic or typical curve. There is a slight initial rise which lasts two or three days unless a new gland is involved, when it will again rise. If the temperature rises during convalescence it indicates either a relapse, which is rare, or complications. The pulse remains slow and does not keep the normal ratio with a rise in temperature. Roux believes this bradycardia is entirely of nervous origin.

The amount of pain and discomfort depends on the extent of the swelling. There is very slight or no pain in a large number of cases. The pain may be intense, especially in persons of nervous temperament. Mastication may cause pain and there is a time-honored tradition that persons suffering from mumps are not able to eat sour articles, such as pickles, etc. This is not so in many cases, but in some patients the sight or mention of lemons or pickles will cause quite severe pain.

Prostration may be very marked in severe cases even before the appearance of complications.

Abdominal pain and slight digestive disturbances may occur. Rare cases of so-called abdominal mumps have been reported in which there is acute abdominal pain with vomiting with the pain localized over the umbilicus. Starr attributes this to appendicitis which he believes is not an infrequent complication of mumps.

The blood has been studied by many observers. There is a slight leukocytosis in all cases. This is due chiefly to an increase in the lymphocytes. Cultures of the blood have always given negative results. Fehling summarizes the blood-picture as follows: There is a slight increase in the number of leukocytes and there is a lymphocytosis which is both relative and absolute. This lymphocytosis is present on the first day of the disease

and persists for about two weeks. The blood changes are of distinct diagnostic value in differentiating mumps from other inflammatory swellings of the salivary glands. He found that the occurrence of orchitis did not invariably alter the blood-picture.

The duration of the swelling in mumps varies from one to six days in the mild cases, to two or three weeks in the severe cases. The course may be greatly prolonged by complications. The parotid gland may resolve very slowly and may even persist for months. Wollstein observed a case in a soldier in which the parotid glands were enlarged for six months and whose mouth washings carried active virus for five and a half months.

Relapses are very rare and have been estimated to occur in from 1 to 6 per cent of all cases. Second attacks may take place but they are most uncommon.

Complications.—These may vary in number and in severity in different epidemics. The great diversity of the complications is due to the fact that the virus reaches the blood stream through the lymphatics and is carried to glands in different parts of the body.

Orchitis.—This is not a common complication in young boys although after puberty it constitutes the most frequent and the most painful complication. It is usually preceded by a rise in temperature and a chill with a great deal of pain. The swelling is usually on one side, although both testicles may be involved. At times one becomes enlarged after the swelling has subsided on the other side. The swelling lasts from three to six days and then slowly subsides. The testicle may become atrophied after the swelling. This atrophy is incomplete and the testicle remains only one-half its original size or it may completely atrophy. Cases have been reported in which the epididymis was involved and the testicle remained normal. It is generally believed that keeping boys with mumps strictly in bed will lessen the probability of this complication.

Pancreatitis.—The pancreas is affected in a small percentage of cases and the symptoms are those of an acute pancreatitis. There is severe abdominal pain with vomiting, nausea and diarrhea. The vomiting may be severe enough to cause hematemesis. The attack generally develops at the end of the first week of the disease and usually lasts about a week. Undigested fat is found in the stools of patients with this complication.

Nephritis.—Albumin can be detected in the urine in many cases during the febrile period, as is the case in other communicable diseases of childhood. A number of observers have found involvement of the kidneys with hematuria, suppressed urine and edema. This nephritis does not last more than a couple of weeks and its course as a rule is benign. A few cases in which a chronic nephritis and death resulted have been reported, but they are extremely rare. The prognosis is usually good in these cases.

Heart.—Endocarditis and pericarditis are complications which may occur and a few have been reported, but they are not nearly so frequent as in other infectious diseases. The pulse may become slow and intermittent.

Respiratory System.—The inflammation in the mouth and tonsils may extend down the respiratory tract and cause pneumonia. These are infections which are not caused by the virus of mumps but the attack of mumps may lower the patient's resistance so that such infections can spread. Edema of the tonsils and larynx are direct complications of mumps and edema of the larynx may prove fatal.

Nervous System.—Meningeal symptoms appear occasionally and have been described by a number of authors. Symptoms on the part of the nervous system are more marked in some epidemics, while in others no such symptoms are observed. Mumps meningitis occurs in children as well as adults. Cases of true meningitis must be differentiated from those in which meningitis symptoms are present but no organic lesion or inflammation of the brain, the so-called meningismus.

Roux, in summarizing his experience, says: "(1) Meningeal symptoms are frequent but typical meningitis is rare. (2) This usually occurs at the height of the disease and sometimes before. (3) There is usually a marked lymphocytosis in the cerebrospinal fluid. (4) There is usually rapid subsidence of the symptoms."

In fatal cases of true meningitis the surface of the brain was found edematous and the sulci filled with a semifibrinous exudate. Cultures invariably proved sterile as did the spinal fluid. In cases presenting focal symptoms, such as twitchings, paralyses, aphasia, hemiplegia, etc., an encephalitis occurred in addition to the meningitis.

The cranial nerves are sometimes involved. This may be the result of pressure from the swollen glands, or the result of absorbed toxin. Those most frequently enlarged are the facial, auditory and subpetrosal nerves. Facial paralysis is usually unilateral and comes on towards the end of the swelling and recovery is always complete. When the subpetrosal nerve is affected there will be a paralysis of the soft palate. Cases of poliomyelitis following mumps have been reported as well as of ascending myelitis.

Polyneuritis involving the peripheral nerves has been noted by several authors. Joffroy had a case of complete flaccid paralysis of all the extremities coming on the twentieth day of the disease accompanied with diminution of the cutaneous sensibility and loss of the deep reflexes. This case made a complete recovery.

The cerebrospinal fluid in cases in which there were no symptoms of meningitis showed a relative lymphocytosis, while in the meningeal cases it contains a great increase in the number of lymphocytes. The fluid is sterile on bacteriologic examination.

The Ear.—The auditory nerve is sometimes affected in mumps, causing a sudden and sometimes permanent deafness which is one of the most distressing complications of this disease. It may occur at any stage of the disease. Hubbard, who made an extensive study of this subject, claims that from 3 to 5 per cent of the deaf-mutes in this country is due to this complication of mumps. The lesion appears to be in the labyrinth and the middle ear is not involved.

The Eyes.—The eyes are occasionally affected and the most serious lesion is optic neuritis, leading in a few months to permanent blindness. The optic nerve atrophies as a result of the toxin of mumps. Congestion of the retinal vessels may lead to temporary disturbances of vision. Conjunctivitis, keratitis and iritis have been observed as complications of mumps. Ruhräh has seen cases of chemosis and edema of the face in which the diagnosis of mumps could have been overlooked on account of the swelling and disfigurement of the face, obscuring the swelling of the parotids.

From the foregoing it is apparent that there are many and diverse complications of mumps and that while the disease in itself is rarely serious, yet the complications and sequelæ may be dangerous. These complications vary in different epidemics. In one, abdominal symptoms may predominate, while in others symptoms on the part of the nervous system are more frequent. The inflammation of the salivary glands in mumps while often intense and very severe rarely if ever goes on to the point of suppuration.

Diagnosis.—When mumps is epidemic the diagnosis is simple. The swelling of the face in which the tip of the lobe of the ear is the central point is sufficient to justify a diagnosis, even though a history of direct exposure cannot be obtained. Cowie claims the appearance around Steno's duct is characteristic of mumps and is not found in any other form of parotitis. The duct sign was found in 96 per cent of the cases that he or his associates had under observation. The changes in the orifice of the duct have been described on page 144.

Confusion in diagnosis is possible when the submaxillary or sublingual glands are enlarged and the parotids normal in size. The history of the case, the presence of an epidemic and the course of the disease shed light on the condition.

Enlargement of the cervical lymph-nodes may cause difficulty at the onset. Here the lobe of the ear is not in the center of the swelling which does not as a rule extend to the face. The swelling is down on the neck and a finger tip can be placed in the fossa just behind the angle of the jaw, which is not possible when the parotid gland is enlarged. Lymphadenitis runs a much longer course and goes on to suppuration in a majority of the cases. The blood-count will be of help. In mumps there will be a slight lympho-

cytosis present, while in adenitis there will be a marked leukocytosis with the polynuclears predominating.

A secondary parotitis can be differentiated by the primary infection and the absence of an epidemic of mumps. Here again the blood-picture will aid in diagnosis. These cases do not run the short typical course and suppuration is not infrequent. This condition sometimes occurs after septic infections and pyemia. A secondary parotitis may follow surgical operations in other parts of the body. It also occurs following or during infectious diseases.

Primary purulent parotitis has been described by many authors. Bretschneider made an exhaustive study of the subject and found it most frequent in poorly nourished children and in premature infants. In almost all of the cases pus could be squeezed out of Steno's duct by pressure on the gland. This is a fatal disease and the mortality in his cases was 69 per cent.

Prognosis.—The prognosis is good in the vast majority of cases and is especially good in young children. The disease itself is self-limited and short in duration. The complications which may assume various forms constitute the danger and fatalities. The sequelæ of blindness, deafness and complete atrophy of the testicles are the most serious, but fortunately are infrequent in early childhood. An uncomplicated case of mumps never ends in suppuration. If it does occur it is a result of secondary infection which should be avoided and which should not be attributed to mumps.

Treatment.—*Preventive.*—Isolation and quarantine are necessary to prevent the spread of this disease. It must be borne in mind that mumps can be communicated two or three days before the appearance of the characteristic swelling. This renders the task of prevention more difficult. The Sanitary Code of the New York State Department of Health gives twenty-one days as the maximum period of incubation and the minimum period of isolation as "two weeks after the appearance of the disease and one week after the disappearance of the swelling." Health regulations in other states do not allow patients to mingle with others until four weeks after the onset of the disease. Very few infections take place after this period. It is a safe rule to isolate children between the second and third week after exposure and not allow them to attend school and keep them under observation. There can be no danger if they attend school for two weeks after exposure. Other children in the family who have had mumps can attend school with safety to others.

Protective.—Hess made some very valuable and interesting experiments in the immunity of mumps. There was an epidemic of mumps in the New York Hebrew Infant Asylum which involved one hundred children. The next year there was a similar epidemic of eighty cases and not one who had contracted the disease in the previous year was infected. Hess attempted to

immunize susceptible and exposed children with blood from children convalescing from the disease. He used 6 to 8 c.c. of blood drawn from the median vein and injected intramuscularly. He obtained the blood from three groups of donors, one who was just recovering from the disease, some from patients who had entirely recovered and some from patients who had had the disease several years before. Not one of the inoculated children came down with mumps, although exposed, and other children in the same ward did. There were no local or constitutional reactions.

Medicinal.—The treatment of mumps is very simple and its course is not influenced by any drugs or treatment known at the present time. The indications for treatment in uncomplicated cases are to relieve pain and to make the child more comfortable. Rest in bed for at least a week is necessary and is the most important treatment. The food should be liquid or soft so that it can be easily swallowed without mastication. Acids and highly seasoned food should be avoided. Milk, custards, junket, eggnog, etc., are easily taken. Children enjoy taking fluids through a straw or glass tube and this is a very useful procedure when there is difficulty in opening the jaw.

A simple saline cathartic can be given at the onset of the disease. Children as a rule take citrate of magnesia or milk of magnesia without difficulty. A mouth wash is necessary, as it is often impossible to cleanse the teeth. If the mouth is dry owing to a lack of saliva, glycerin should be added to the mouth wash. Dobell's solution, Seiler's solution, listerine, alcohol, lavoris, etc., when sufficiently diluted make excellent mouth washes. There may be excessive salivation and this can be relieved by full doses of atropin.

The amount of pain in the gland varies with different patients. Many do not complain of pain, while others suffer intensely. Heat gives relief in some cases and a hot water bottle or electric heater is a great comfort. Other patients find ice applications more effective in relieving the pain. Local applications of hot camphorated oil, belladonna ointment, lead and opium wash all tend to relieve the pain.

Internally the use of antipyrin, allonal or codein will make the patient more comfortable. The treatment of orchitis is important. The patient must remain absolutely quiet in bed with the testicle supported by a jock strap and cotton. Ice applications give the greatest relief. The usual course of this complication is from six to nine days.

Lumbar puncture should be used in cases of meningeal symptoms.

For edema of the glottis the only relief is a prompt tracheotomy. When the throat and uvula become edematous the tissues should be scarified with a sharp knife.

Public Health Regulations.—Mumps is a reportable disease and the local health officer must be notified at once. Strict quarantine is not required

in New York State but the child should be isolated for two weeks after the appearance of the disease and one week after disappearance of the swelling. The patient is excluded from school for this period.

The present status of mumps is outlined in the following report of a special committee of the American Public Health Association:

1. INFECTIOUS AGENT.—Unknown.

2. SOURCE OF INFECTION.—Secretions of the mouth and possibly of the nose.

3. MODE OF TRANSMISSION.—By direct contact with an infected person or with articles freshly soiled with the discharges from the nose or throat of such infected person.

4. INCUBATION PERIOD.—From twelve to twenty-six days. The most common period, eighteen days, accepted as usual. A period of twenty-one days is not uncommon.

5. PERIOD OF COMMUNICABILITY.—Unknown, but assumed to persist until the parotid gland has returned to its normal size.

6. METHODS OF CONTROL

   (a) The infected individual and his environment

   1. *Recognition of the Disease.*—Inflammation of Stenson's duct may be of assistance in recognizing the early stage of the disease. The diagnosis is usually made on swelling of the parotid gland.

   2. *Isolation.*—Separation of the patient from nonimmune children and exclusion of the patient from school and public places for the period of presumed infectivity. (See 5.)

   3. *Immunization.*—None.

   4. *Quarantine.*—None. Exposed susceptible persons should be regularly inspected for the onset, the presence of initial symptoms of the disease, such as fever, or swelling or pain of the parotid or adjacent lymph glands, for three weeks from the date of last exposure.

   5. *Concurrent Disinfection.*—All articles soiled with the discharges from the nose and throat of the patient.

   6. *Terminal Disinfection.*—None.

   (b) General measures—None.

CHAPTER X

DIPHTHERIA

Diphtheria is an acute infectious disease caused by the diphtheria bacillus and characterized by a local fibrinous exudate, usually upon a mucous membrane, with intense local inflammation and a general toxemia.

HISTORY

Diphtheria, described by the ancients, is an important subject of research at the present time and its study has led to epoch-making discoveries in medical science. Egyptian or Syrian ulcer is described by Aretæus (second century) in a clinical picture which may be recognized as diphtheria. The accounts of severe epidemics in Spain during the seventeenth century, given with admirable detail, to which the terms *morbus suffocans* or *garrotillo* were applied, show that they were dealing with a severe form of epidemic diphtheria. These early Spanish writers recognized the epidemic nature of the disease, the difficulty in swallowing, the membrane in the throat and the glandular enlargements. At the same time the term *male in canno* was applied to similar severe epidemics in Italy and Sicily. During the eighteenth century epidemics of throat inflammations were described in England, France and America. In 1771, Bard, professor of the practice of physic in King's College (now Columbia University), in a notable memoir described the disease as *angina suffocativa,* considered it of an infective nature and advised removal of the unaffected children when a case occurred in a family. In some of the descriptions of the epidemic throat inflammations, mention of scarlet rashes and severe throat ulceration indicate that scarlet fever was not differentiated from diphtheria.

The foundation of modern knowledge was laid by Bretonneau (1778-1862), who in 1826 published a book of 540 pages, *Des inflammations speciales du tissu muquex et en particulier de la diphthérite,* which was a complete clinical description of the disease. He established a differential diagnosis of throat inflammations and originated the term *diphthérite* to represent his conception of the specificity of the pellicular exudate of the affected part. His final publication in 1858 uses the term "diphthérie." During the half century which followed, other investigators took exception to his work, but it was placed upon an irrefutable basis by Löffler in 1884.

Following Bretonneau, experimental and pathological work was continued actively, but the next great contribution was made by Klebs and Löffler in 1883 and 1884. In 1883 Klebs announced with confidence that small bacilli, staining irregularly with methylene-blue, were the causative factors in diphtheria. The next year his assistant, Löffler, published his epoch-making work which stimulated immense activity in the whole field of bacteriology. He isolated the bacillus described by Klebs, did extensive animal experimentation, perfected the Löffler's methylene-blue stain and the blood-serum medium, noted puzzling phenomena which further work on immunity has elucidated, and laid broad outlines for succeeding research. His conservative conclusions were that it could not be disproved that the bacillus described by Klebs was the causative factor in diphtheria, but that further investigation should be made of the chemical poison which constitutes an important factor in the pathogenesis.

Roux and Yersin (1888-1890) whose discovery of the toxin of diphtheria was a brilliant scientific achievement, confirmed Löffler's work. Nearly coincident with this, Behring and Fränkel (1890) published the results of their experiments to produce an artificial immunity to diphtheria and its toxin. Their ability to produce immune serum against tetanus, and Behring's diphtheria antitoxin opened the field of serum therapy. To Behring belongs the credit of the discovery of diphtheria antitoxin.

Following this began the therapeutic use of antitoxin, which called for a standardization of the preparations. Ehrlich, whose unit of antitoxin is in general use, did notable work in establishing such standards.

In 1913 Schick applied to man the method of demonstration of individual natural immunity which has been useful in the prevention of diphtheria. Research in diphtheria is still an active field of scientific endeavor.

ETIOLOGY

The causative organism of diphtheria is *Bacillus diphtheriæ* or the Klebs-Löffler bacillus. The more descriptive name *Corynebacterium diphtheriæ* has been accepted by the Society of American Bacteriologists. It is highly infectious, endemic and epidemic, but its incidence is influenced by several factors in which age and natural immunity play an important part.

Age and Natural Immunity.—Children under six months of age retain a passive immunity transmitted from their mother's blood. Determination of immunity by the Schick test has demonstrated that city children have a greater immunity than those living in the country. Zingher believes that this is due to a natural antitoxin built up through repeated transient infections on the part of children living in crowded quarters.

Park estimates the age table of susceptibility as follows:

TABLE XVI.—AGE TABLE OF SUSCEPTIBILITY TO DIPHTHERIA AS INDICATED BY THE POSITIVE SCHICK DIPHTHERIA-TOXIN STAIN TEST

Age	Country, Per Cent	City, Per Cent
Under 3 months	30	15
3 to 6 months	50	30
6 months to 1 year	80	60
1 to 2 years	85	70
2 to 3 years	75	55
3 to 5 years	70	40
5 to 10 years	65	30
10 to 20 years	60	20
Over 20 years	50	15

The ages of fatal cases as reported to the New York State Department of Health in 1915 to 1924 show that two-thirds of all fatal cases occur in children under five years of age.

TABLE XVII.—DEATH RATE FROM DIPHTHERIA PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1924, ACCORDING TO AGE

Age, Years	Number		Rate		Per Cent of All Cases	
	1915	1924	1915	1924	1915	1924
Under 1.............	186	72	163.0	30.8	.8	.4
1	396	198	212.7	92.6	7.5	6.4
2	268	144	135.2	65.6	13.2	9.6
3	219	142	112.5	64.5	17.0	15.6
4	189	138	101.1	64.5	21.1	17.4
Under 5.............	1258	694	....	...	...	...
5-9	366	268	40.9	25.5	13.4	10.4
10-14	69	46	8.1	4.8	3.9	2.5
15 and over..........	77	75	1.1	.9	.1	.1
TOTAL ALL AGES...	1770	1083	17.9	9.8	1.2	.8

Deacon made a study of 31,028 cases and 2,458 deaths from diphtheria reported to the Michigan Department of Health. He found that one-half of the cases were less than nine years of age, with the average at eight years and eleven months. One-half of the deaths occurred at four years and eight months. The highest single year of age for all cases was the sixth, and the highest single year for deaths was the third. The group under one year of age gave only 0.7 per cent of the cases, but furnished 5.5 per cent of the deaths. This group showed a fatality rate of 61.9 per cent. This rate is reduced to 34.7 per cent for the one-year group and to 21.4 per cent for the two-year group.

The mortality statistics relating to diphtheria in New York State for the ten-year period 1915-1925 show that there are approximately twice as many deaths in the cities as in the country districts. There has also been a

marked decrease in the number of deaths since 1922, both in the urban and rural communities, but the ratio of deaths between the city and the country remain the same.

TABLE XVIII.—DEATH RATE FROM DIPHTHERIA PER 100,000 POPULATION FOR UNITED STATES DEATH REGISTRATION AREA OF NEW YORK STATE FROM 1915 TO 1925

Year	United States Registration Area	New York State	New York City	New York State Exclusive of New York City
1915	15.7	17.9	24.5	10.5
1916	14.5	15.2	19.4	10.5
1917	16.6	17.3	21.4	12.6
1918	13.9	17.4	22.7	11.2
1919	14.7	19.9	22.2	17.2
1920	15.3	18.2	18.5	17.8
1921	17.7	16.1	15.7	16.5
1922	14.6	13.5	15.2	11.6
1923	12.1	9.3	9.6	8.9
1924		9.8	12.2	7.1
1925		9.0	11.2	6.4

Individual susceptibility is an important factor in the spread of the disease. Persons may harbor in their throats diphtheria bacilli of a virulent type without contracting the disease, and many who are exposed escape. For those who are susceptible one attack does not confer lasting immunity.

Season.—There is a sharp increase in the number of cases in the fall, which is referable to the assemblage of the children in schools.

Table XIX gives the number of cases reported in New York State according to months and shows a much larger number of cases in the winter months when the children are congested in schools, etc., and a sharp decrease of cases in the summer months. This is also seen in the fatal cases.

TABLE XIX.—MORBIDITY FROM DIPHTHERIA PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1925, ACCORDING TO MONTHS

Year	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1915	236.9	258.3	246.3	205.2	205.8	241.9	164.8	120.9	135.4	213.1	252.1	242.7
1916	255.3	235.2	232.9	205.6	253.7	242.6	167.2	97.6	97.7	146.2	170.9	189.0
1917	202.8	221.0	205.5	191.2	199.0	190.2	151.5	117.4	143.8	228.6	227.1	198.9
1918	176.3	160.8	178.3	196.5	80.1	191.1	141.4	94.1	97.7	150.0	153.9	89.1
1919	253.3	266.4	277.6	245.1	260.0	243.7	159.8	136.5	171.8	263.5	298.9	337.4
1920	290.7	219.2	242.4	228.8	234.5	232.4	147.6	110.0	119.1	221.8	396.0	404.6
1921	387.8	413.8	320.6	287.5	262.3	259.5	123.3	119.7	141.1	213.2	280.4	267.9
1922	241.4	208.7	198.2	188.2	205.0	165.7	114.7	99.2	103.7	163.0	221.1	204.9
1923	182.1	144.7	131.0	126.4	132.3	122.9	103.7	71.4	88.1	158.1	209.8	191.8
1924	194.3	174.2	154.1	158.0	165.0	166.4	120.4	79.7	82.3	105.0	133.0	162.8
1925	144.0	142.6	147.8	171.7	165.6	147.3	88.5	59.8	62.2	98.4	105.7	110.9

TABLE XX.—MORTALITY FROM DIPHTHERIA PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1925, ACCORDING TO MONTHS

Year	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1915.....	21.3	23.3	25.2	18.4	21.0	19.6	14.4	11.2	9.8	14.1	16.1	20.2
1916.....	22.8	20.9	20.3	18.4	19.5	15.8	11.6	8.4	7.9	9.3	13.4	14.6
1917.....	19.2	20.2	20.7	20.8	16.6	17.2	12.4	9.9	12.4	17.7	20.2	21.0
1918.....	19.7	19.1	20.1	24.5	18.4	15.8	12.1	9.1	10.0	22.0	16.7	20.9
1919.....	25.6	29.8	26.4	23.4	24.0	15.5	10.1	9.1	12.7	15.2	22.1	25.3
1920.....	26.8	30.1	25.6	19.8	15.4	14.8	8.4	8.4	7.7	15.4	20.9	25.9
1921.....	24.4	28.7	18.1	16.5	16.0	15.0	9.2	9.1	9.4	11.2	16.8	19.2
1922.....	19.1	24.5	18.7	18.4	14.8	12.0	9.0	6.2	6.7	8.5	12.3	13.1
1923.....	15.9	14.5	7.4	10.2	8.2	7.8	6.2	5.3	5.0	8.6	12.5	9.9
1924.....	12.2	13.7	13.3	11.6	10.8	9.7	7.9	6.1	4.9	7.1	9.1	11.6
1925.....	10.5	9.5	10.4	14.5	13.7	10.7	6.6	4.3	5.7	6.1	8.2	7.5

Sex has practically no influence in the death rate, as is shown in Table XXI. There is a slight predisposition among boys who come into closer contact in their games, etc., than do the girls.

TABLE XXI.—DEATH RATE FROM DIPHTHERIA PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1924, ACCORDING TO SEX

Year	Male	Female
1915	19.1	17.0
1916	15.9	14.8
1917	18.0	16.9
1918	19.2	15.6
1919	20.8	19.0
1920	19.3	17.2
1921	16.7	15.5
1922	14.1	13.1
1923	9.3	9.3
1924	10.5	9.2

Mode of Transmission.—The most important modes of transmission are: (1) Directly from person to person through the local discharges. All contacts, including doctors and nurses, need to exercise the greatest precaution against receiving infecting material on their persons. (2) Recently infected articles may carry the microörganisms. Toys, pencils, handkerchiefs, drinking cups, and other articles that have been in the mouth or to the nose of a diphtheria case may be a source of infection. (3) Atypical cases of tonsillitis, otorrhea, and the so-called "larval cases" may harbor virulent diphtheria bacilli. (4) Healthy carriers who have not had the disease but who have been in contact with it may retain the organism in their throats. (5) Healthy persons who have not been exposed to diphtheria sometimes carry virulent bacilli in their throats. (6) Epidemics have been traced to milk, either through contamination or, rarely, through diphtheritic lesions on the cow's udder. The presence of diphtheria bacilli in animals is extremely rare.

BACTERIOLOGY

The diphtheria bacillus is a non-motile, non-flagellated, non-spore-forming aërobe. It will grow under anaërobic conditions in the presence of suitable carbohydrates. It is killed by boiling it about one minute, but it is resistant to cold and will withstand freezing. It is easily killed by chemical disinfectants in the strengths customarily employed, but is resistant to the effects of drying and light, if it is protected by a film of mucus or membrane.

The bacilli are slender, straight or slightly curved rods from one to six micra in length. They are usually clubbed at one or both ends. They occur singly or in pairs, and when paired may lie side by side or at an angle, but never in chains. This is because the diphtheria bacillus "snaps" in dividing instead of slipping or sliding apart as apparently all species of bacteria except the diphtheria group do. They exhibit a number of morphological variations which have not been correlated with such biological variations as virulence, toxicity, etc. They stain with aqueous aniline dyes. Stained with Löffler's methylene-blue the important diagnostic points of banding, chromatic polar bodies and irregular staining are demonstrated.

They grow readily upon most of the richer laboratory media, but develop most readily upon those that have a meat infusion for their basis. The one most widely used is Löffler's blood-serum medium upon which the bacilli develop minute grayish-white glistening colonies within twenty-four hours. These rapidly outstrip the accompanying streptococci colonies. The medium has almost selective powers for the diphtheria bacilli.

For diagnosis, cultures from suspected throats and noses are taken on Löffler's blood-serum medium and incubated at 37° C. for twelve to eighteen hours. At the end of that time Löffler's methylene-blue stain will demonstrate the irregular staining and characteristic morphology of the Klebs-Löffler bacillus. The polar bodies may be shown by the Neisser stain. Occasionally it is possible to make a bacteriological diagnosis without a culture by means of a microscopical examination of a direct smear from the throat stained in the usual way.

The diphtheria bacillus through its toxins is pathogenic for the ordinary laboratory animals, except rats and mice. Dogs, cats, fowl, rabbits and guinea-pigs, are susceptible. These animals, however, are not a source of infection, as the disease occurs in them rarely. A few cases have been reported of diphtheria in cats and dogs. Injection of a broth culture in guinea-pigs produces nephritic symptoms, congestion of lungs, liver, spleen and kidneys. A severe congestion of the suprarenals is pathognomonic of diphtheritic intoxication.

There is a wide variation in the virulence of different strains of the bacilli, the determination of which is sometimes of great importance when

diphtheria-like organisms are isolated from atypical cases or from supposed diphtheria carriers. Public health laboratories which serve the physician for diagnosis are usually equipped to make a virulence test. One method is by the subcutaneous injection of 2 c.c. of a forty-eight-hour broth or ascitic broth culture into a normal guinea-pig. This dose will kill the animal in from three to five days if the culture is virulent. A control injection is made into another pig of the same weight which has previously received a protecting dose of antitoxin. "In our opinion the evidence clearly supports the view that a strain non-virulent to guinea pigs is non-virulent to man and that a strain virulent to guinea pigs in whatever degree is virulent to man, but not necessarily in the same degree. This information derived from guinea pigs may be applied safely to the study of diphtheria in man." (Diphtheria Medical Research Council, page 323.)

B. diphtheriæ produces an exotoxin which accounts for the severe systemic reaction when the microörganisms are limited to the local lesion. When grown upon the ordinary nutrient broth it produces a soluble toxin which retains its potency even in a sterile filtrate. A meat infusion broth with the addition of 1 to 2 per cent peptone, slightly alkaline in reaction, at a temperature of 37° C. with free access of oxygen furnishes a satisfactory medium for toxin production. The maximum yield of toxin is obtained after five to eight days. Careful research has not yet revealed its chemical composition. In fluid form it is destroyed by a temperature of 58° to 60° C. It deteriorates by exposure to air and light. Different strains vary markedly in their toxin production.

The introduction of toxin into a susceptible animal stimulates the production of antitoxin which remains in the blood-serum and retains its power to neutralize toxin for some months. This is the basis of the commercial production of antitoxin. Horses are commonly used, as they develop a large amount of antitoxin and endure the frequent bleeding very well. Successive subcutaneous injections of toxin in ascending doses are made at intervals of from five days to a week until the blood-serum contains a satisfactory amount of antitoxin. By giving a three months' resting period after nine months of immunization, horses may furnish antitoxin for several years.

To obtain the serum a sharp cannula is introduced into the jugular vein and from 5 to 8 liters of blood are withdrawn under aseptic conditions. The bleeding may be repeated as often as once a month. The serum is allowed to separate, is refined and concentrated and then standardized as to units per cubic centimeter. All of the antitoxin products on the market are tested at intervals for potency and purity by the United States Public Health Service. Many public health departments furnish it without charge for prophylactic and therapeutic use.

The Schick Test.—The fact that some persons may be in contact with diphtheria and still not contract the disease is due to antitoxin having developed in their own blood. Schick in 1913 published a description of a simple clinical test by which the presence or absence of antitoxin may be demonstrated. Minute quantities of diphtheria toxin produce an irritant effect when injected intracutaneously. If the subject possesses sufficient natural antitoxin to protect him from the disease, that amount will neutralize the toxin injected and no irritation will occur. If not, a positive reaction will occur within from twenty-four to ninety-six hours.

Park states that over a million tests made in the past thirteen years have proved without doubt that Schick developed an accurate and reliable test for the presence or absence of diphtheria toxin in the body. This simple test has given us much valuable information about susceptibility to diphtheria and pointed out some practical and workable methods for the control of the disease. A positive reaction to a Schick test indicates that the person is susceptible to diphtheria. The technic of this test which has been named after its discoverer will be discussed later.

PATHOLOGY

In order to have an understanding of the tissue injury produced by infection with the diphtheria bacillus, one must keep in mind the powerful soluble toxin which it elaborates and diffuses through the blood stream, as well as the local injury it produces. In this production of exotoxin it is paralleled only by tetanus bacillus which produces a powerful systemic effect but has little power to produce local lesions.

Local Effects.—The most frequent sites of infection are the tonsils, epiglottis, larynx and uvula. The characteristic lesions are those occurring upon a mucous membrane. From two to five days after they gain a foothold upon the mucosa they have multiplied until grayish spots are visible upon an intensely congested base. These enlarge, thicken and coalesce to form an elevated, grayish pseudomembrane which is quite adherent to the underlying tissue. When the pseudomembrane is peeled off it leaves a bleeding surface upon which a new false membrane quickly forms. The first step is in the destruction of the superficial cells of the mucosa which undergo degeneration and necrosis. From the structures below, an inflammatory exudate is poured out which permeates the dead cells and spreads upon the surface. The formation of fibrin in the exudate both upon the surface and among the dead cells forms the organized false membrane. Numerous leukocytes are poured out and there is some hemorrhage. The further accumulation of leukocytes between the exudate and the deeper tissues leads to a digestion of the fibrin and the final separation of the membrane. "Ease of detachment
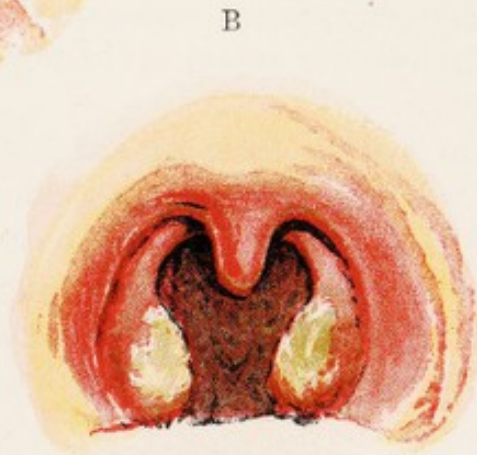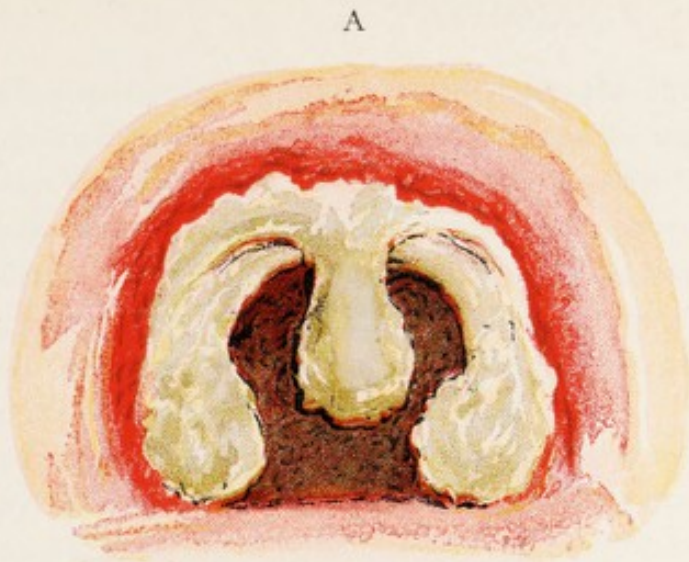
PLATE II.—THE DIPHTHERITIC MEMBRANE

A.—Severe pharyngeal diphtheria (fatal case).
B.—Typical tonsillar diphtheria.
C.—Pseudodiphtheria. The specimen is seen from behind, the larynx and trachea having been laid open, and shows an extensive membrane involving the epiglottis and the entire lower pharynx, but extending into the larynx only a short distance. It is also seen upon the posterior surface of the uvula and soft palate, the tonsils being only partially covered. The color of the membrane is not characteristic of pseudodiphtheria, as the same appearance is often seen in true diphtheria, particularly of the septic type.

depends apparently to a large extent upon the variety of epithelium involved in the pathological process. Where this epithelium is of a stratified squamous character the false membrane offers some considerable resistance to forcible removal, whereas in mucous membranes covered with stratified ciliated columnar epithelium the attachment is much less tenacious, the false membrane being easily detached, or, indeed, spontaneously expelled from the body in the form of a partial or complete cast of the affected part." (Diphtheria Medical Research Council, page 217.)

In fatal cases the membrane may become very extensive and a dirty green or gray with a characteristic odor. The parts may even become gangrenous. The nose may be entirely blocked by the membrane, or it may extend into the trachea, bronchi and bronchioles.

The enlargement of the *cervical glands* may be considered as a part of the local effect, and is roughly proportionate to the severity of the infection.

The *lungs* are involved in about 60 per cent of the cases (131 out of 220 Boston cases of Councilman). Bronchopneumonia with serous, cellular, fibrinous or hemorrhagic exudate is characteristic. This occurs by direct extension from the laryngeal involvement, and in many cases is due to streptococci which pass into the bronchi.

Distant Effects.—The remote sequelæ of the infection which is attributable to the toxin carried by the blood stream are often of graver import than the local effects. The heart and nervous system show the greatest damage, but the liver, kidneys and adrenals share in the injury. On the other hand, individuals with a small amount of antitoxin in their blood may develop diphtheria but be protected by the antitoxin from the severe toxic effects. Death may take place at the height of the toxemia, evidently from the effect upon the heart and circulation.

The *heart* may be seriously affected both early and late in the disease. Both the muscle-fibers and the interstitial tissues may be involved, but no characteristic lesion has been found. Fatty degeneration of the myocardium is a frequent occurrence. Romberg in 1891 advanced the theory that a logical explanation of the circulatory disturbances was the assumption of a paralysis of the vasomotor center with a resulting splanchnic congestion at the expense of the rest of the body. Other investigators have considered damage to the special conducting area of the heart. Sudden death may be due to degenerative changes in the vagus.

The *liver* is the seat of cloudy swelling, and, at times, large or small areas of focal necrosis.

The *kidneys* show the changes common to other severe infections. The nephritis may range from cloudy swelling to a severe acute type. The parenchymatous changes are more severe than the interstitial. Albuminuria is common.

The *adrenals* rarely show gross lesions in man, but in animals they are characteristic, a fact that has led to detailed histological studies with contradictory results. The Medical Research Council concludes (page *222*) that the main action of diphtheria toxin is on the heart, aided by serious damage to various organs which contribute to the maintenance of the circulation, and that no doubt the vasomotor centers and the chromaffin tissues are involved in the damage.

The Nervous System.—Paralysis occurs in about 20 per cent of all cases of diphtheria. The nerves associated with the paralyzed areas show degenerative changes, the fibers are swollen, and the medullary sheath filled with fine or coarse granules, while the axis cylinder may persist for some time before degeneration. The ganglion-cells usually escape serious injury, which accounts for the complete recovery which may be expected. The nerves which supply the palate and larynx, those of the extrinsic muscles of the eye, and the muscles of accommodation suffer especially. Walsh considers that while paresis of the muscles of accommodation and generalized peripheral neuritis are probably due to a hematogenous intoxication of the nervous system, there are distinct local paralyses corresponding with the site of the infection which ascend as a perineural lymphatic intoxication to the corresponding cranial or spinal ganglion-cells. The paralysis is, therefore, of central origin, but is distributed according to the source of the toxin.

SYMPTOMS AND CLINICAL COURSE

Diphtheria may range in severity from cases so mild as to pass for a catarrhal pharyngitis to malignant cases in which the child is *in extremis* within the first twenty-four hours. The symptoms may remain purely local in their manifestations, or there may be severe systemic disturbances. In general the extent of the membrane is an index to the amount of systemic toxemia, but the location of the membrane in the larynx where the blood supply is relatively poor gives rise to less toxemia than pharyngeal diphtheria where the toxin can be absorbed from the highly vascular mucous membrane. The prompt administration of antitoxin aborts the course of the disease to such a degree that the practitioner rarely sees the dramatic advanced cases common a few decades ago, except where the child has been deprived of appropriate treatment through the ignorance of its parents or through the willful neglect practiced by some of the healing cults.

The *onset* occurs from one to five days after exposure, or possibly it may be delayed to seven days. After a preliminary feeling of malaise and a slight sore-throat the temperature gradually rises until it reaches a maximum of 103° to 104° F. The membrane appears in the throat and the cervical glands become enlarged. This may be a marked feature of the

disease. On the other hand, the physician frequently sees an abrupt onset with vomiting, headache, chilliness and a temperature that climbs rapidly to 103° to 104° F. within the first twenty-four hours. In young children convulsions may be a feature of the onset.

Pharyngeal Diphtheria.—The typical case begins as a sore-throat, with redness of the fauces and slight difficulty in swallowing. The tonsils are swollen and at first covered with a patchy exudate which cannot be definitely differentiated from a tonsillitis by inspection. By the third day, if the course is uninterrupted by the administration of antitoxin, the membrane has covered the tonsils, the fauces and perhaps the uvula. All of these structures are edematous and congested, and the cervical glands are swollen and may be tender. There is mechanical difficulty in swallowing, with a feeling of stiffness. Even with a lesion as extensive as this the constitutional symptoms may be fairly mild, with a temperature range from 102° to 103° F. The pulse range is from 100 to 120. By the fifth day the membrane begins to separate at the edges, and from the seventh to the tenth day the throat has become clear of membrane and the swelling reduced. The membrane may never form a complete exudate or it may become so extensive as to involve the larynx and the nose and be accompanied by severe constitutional symptoms with a marked septicemia.

The severe constitutional symptoms as a rule appear when the pharyngeal exudate is at its height. This marks the point when the maximum amount of toxin has been discharged into the blood stream before the defense mechanism becomes effective. Whenever there is an extensive membrane with a sloughing, fetid condition, one may expect extreme prostration, frequent small pulse, high fever, nervous symptoms, an ashen-gray face and general lymphatic enlargement. A subnormal temperature is an unfavorable symptom. A leukocytosis and an albuminuria are to be expected.

Nasal Diphtheria.—The localization of the membrane in the nose presents a malignant type of the disease. The nostrils are occluded by the membrane from which an irritating serosanguineous discharge oozes over the lips. The adenitis is usually intense, owing to the rich lymphatic supply of the nasal mucosa. The membrane may extend into the middle ear, the antra, or through the tear-ducts into the conjunctiva. The systemic toxemia is profound. However, it is possible to have a mild nasal diphtheria.

A *membranous rhinitis* in which the offending organism may be the Klebs-Löffler bacillus is an unusual affection, usually seen in children, in which the nares are entirely occupied by a thick membrane with an entire lack of constitutional symptoms. The disease runs a benign course, and other children in the family are seldom infected.

Laryngeal Diphtheria.— This is one of the group of conditions known as membranous croup. In a large percentage of the cases of membranous

laryngitis the *Bacillus diphtheriæ* is the offending organism. Osler gives the following picture of membranous laryngitis:

The affection begins like an acute laryngitis with slight hoarseness and rough cough, to which the term croupy has been applied. After these symptoms have lasted for a day or two with varying intensity the child suddenly becomes worse, usually at night, and there are signs of impeded respiration. At first the difficulty in breathing is paroxysmal, due probably to more or less spasm of the muscles of the glottis. Soon the dyspnoea becomes continuous, inspiration and expiration become difficult, particularly the latter, and with the inspiratory movement the epigastrium and the lower intercostal spaces are retracted. The voice is husky and may be reduced to a whisper. The color gradually changes and the imperfect aëration of the blood is shown in the lividity of the lips and finger-tips. Restlessness comes on and the child tosses from side to side, vainly trying to get breath. Occasionally, in a severer paroxysm, portions of membrane are coughed out. The fever in membranous laryngitis is rarely very high and the condition of the child is usually good at the time of the onset. The pulse is always increased in frequency and is small if cyanosis be present. In favorable cases the dyspnoea is not very urgent, the color of the face remains good, and after one or two paroxysms the child goes to sleep and wakes in the morning, perhaps without fever and feeling comfortable. The attack may recur the following night with greater severity. In unfavorable cases the dyspnoea becomes more and more urgent, the cyanosis deepens, the child, after a period of intense restlessness, sinks into a semi-comatose state, and death finally occurs from poisoning of the nerve centers. In other cases the onset is less sudden and is preceded by a longer period of indisposition. As a rule, there are pharyngeal symptoms. The constitutional disturbance may be more severe, the fever higher and there may be swelling of the glands of the neck. Inspection of the fauces may show the presence of false membrane on the pillars or on the tonsils. Bacteriological examination can alone determine whether these are due to the Klebs-Loeffler bacillus or to the streptococcus.

In infants, even with prompt modern treatment, the prognosis in laryngeal diphtheria is poor, the mortality ranging from 25 to 40 per cent. The progress is rapid and may reach a fatal termination within thirty-six to forty-eight hours after the first appearance of symptoms. In older children the course is slower and may end in a bronchopneumonia in from two to five days.

Malignant Diphtheria.—This form is characterized by severe symptoms from the outset, with an extensive membrane, gangrenous or dark from hemorrhagic infiltration, which fills the entire pharynx and extends into the adjacent parts. There may be sloughing of the tonsils, uvula or soft palate. There is often an abundant offensive nasal discharge. Extensive infiltration of the cellular tissue of the neck and the cervical lymph glands may cause the head to be thrown back to relieve pressure upon the larynx and trachea. The swelling may fill out the whole space beneath the jaw from ear to ear. Pressure upon the jugular veins leads to congestion of the

face and brain. In this form the temperature is usually high and fluctuating. Any of the symptoms which characterize an acute toxic condition may occur. The pulse is weak and rapid and the circulation poor. Vomiting and diarrhea often occur. Nervous symptoms vary from excitement and delirium to apathy and stupor. Nephritis usually complicates this form and the urine shows albumin and casts in large amounts. Death may occur from invasion of the larynx, from nephritis, from bronchopneumonia, but most frequently from cardiac failure. If death does not occur at the height of the local lesions it may result later from sloughing of the tissues of the neck or throat followed by hemorrhage, from a late nephritis, pneumonia, or paralysis of the heart or respiration.

Diphtheria of Other Parts.—Diphtheria bacilli have been found in conjunctivitis, which is catarrhal in character or associated with slight membrane formation. The infection may spread to the conjunctiva from the nasal mucosa. Diphtheria of the external auditory meatus may accompany diphtheritic otitis media. Diphtheria of the skin occurs in severe cases of pharyngeal diphtheria by extension of the affection from the lips to the skin of the adjacent portions of the face. It may occur about the anus. Pseudomembranous inflammations on ulcerated surfaces and wounds are usually due to streptococcic infections, but in some cases the Klebs-Löffler bacillus is found. Diphtheria of the vulva is sometimes reported.

COMPLICATIONS AND SEQUELÆ

The general use of antitoxin has had the paradoxical effect of increasing the number of cases which show complications and sequelæ, because the treatment prolongs the lives in severe cases which would otherwise succumb to the disease. Of the local complications, hemorrhages from the nose or throat are not uncommon. Otitis media due either to the *Bacillus diphtheriæ*, or more frequently to secondary invaders, occurs particularly in the rhinopharyngeal cases. Bronchopneumonia is a frequent complication in severe cases, and especially in the laryngeal type. Emphysema occurs less frequently.

The Heart.—Myocarditis, present in some degree in nearly all severe cases, may cause no distinctive symptoms, but may be detected by physical examination. Pericarditis and endocarditis are rare. Heart-failure during or after diphtheria is due to several different causes, some very obscure. The heart symptoms are more common in the second or third week of the disease. A recognized syndrome, suggestive of vagus involvement, relates to the stomach, heart and respiration. About the end of the second week the patient refuses food and vomits without apparent cause. Attacks of severe epigastric pain come in paroxysms. The pulse rate drops from 110

or 120 to 80 or below, and becomes compressible and somewhat irregular. Dyspnea and cyanosis are moderate in the beginning, but increase in severity. These symptoms, if severe, grow progressively worse and may terminate in death within twenty-four hours. The same group of symptoms may occur in mild form and disappear, but more frequently they are the beginning of the serious form of complication. The late cases of this syndrome are usually associated with some other form of postdiphtheritic paralysis.

The heart-failure that occurs at the height of the disease is sometimes due to cardiac thrombosis. When it occurs late, after convalescence is well established, it is probably due to muscle degeneration—a true myocarditis.

In addition to the local hemorrhages, subcutaneous hemorrhages occur in severe cases, ranging in size from petechiæ to extensive extravasation.

Anemia, often severe and persistent, usually follows diphtheria.

The Kidneys.—Albuminuria is the rule in cases of moderate severity. If acute nephritis occurs it develops at the height of the local disease. Chronic nephritis is a rare sequel.

Postdiphtheritic Paralysis.—This is an important sequel of diphtheria. It is due to the action of the unneutralized toxin upon the nerves, and its occurrence is conditioned both by the severity of the infection and the lapse of time before the administration of the antitoxin. Rolleston found some form of paralysis in 20.7 per cent of 2,300 cases observed by him. He classified 2,250 faucial cases in six groups from very severe to very mild cases, and found that the percentage of the paralysis increased with the severity of the case. In very severe cases 70 per cent showed paralysis, in his mild cases only 2 per cent, and his very mild cases had no paralysis. Those given antitoxin on the first day of the disease developed paralysis only in 3.6 per cent of cases, on the second day in 19.09 per cent, while cases not receiving antitoxin until the third to the sixth day, in from 21 to 27 per cent.

During the first two or three weeks of the disease the palsies which occur are those of the palatal nerves and the vagus. During the third week ocular manifestations may occur. These are most frequently a paralysis of the muscles of accommodation, shown by inability to read, but internal strabismus may occur, while dilatation of the pupils and ptosis are rare. Loss of accommodation may not be detected in very young children.

From the fifth to the eighth week the generalized paralyses develop, rarely before or after that time. The muscles of the eyes, the pharynx and the palate may be affected. In severe cases the muscles of the extremities, trunk, neck and even the diaphragm may be involved. Pain is rare. Great difficulty is shown in swallowing, and food may cause violent coughing or an aspiration pneumonia.

Respiratory paralysis is usually a later development which follows exten-

sive paralysis elsewhere. It is more frequently due to an involvement of the phrenic than the intercostal nerves. It begins with attacks of dyspnea which increase in severity until respiration depends upon the conscious efforts of the patient. This condition may last for several hours and then return after a short time. Death is a frequent termination. The heart may continue to beat regularly even when the breathing is much disturbed, but an irregular, intermittent pulse, either abnormally rapid or slow, is more usual. There may be vomiting and abdominal pain. Death is the result of either circulatory or respiratory failure.

The duration of the paralysis is only from two to three weeks, so that if the patient can be kept alive during the critical period recovery may be expected.

Paralysis of the extremities is seldom complete, and usually begins to improve by the end of the second week.

Diphtheria with Other Diseases.—Virulent diphtheria bacilli are sometimes found in the throat of a scarlet fever patient, and the spirilla and fusiform bacillus of Vincent's angina are sometimes prominent features of direct smears from the throat of a diphtheria patient.

DIAGNOSIS

The clinical diagnosis of a typical case of diphtheria presents few difficulties, but in mild cases and in the early stages the bacteriological evidence is of great importance, since its presence is the sole criterion of true diphtheria. The infection may range in severity from a simple catarrhal inflammation to a sloughing gangrene. It must also be remembered that occasionally a membranous inflammation is the result of other organisms, such as the streptococcus, pneumococcus, staphylococcus, Friedländer's bacillus, Vincent's organisms and *Bacillus pyocyaneus*.

Clinical Diagnosis.—The mode of onset varies so widely as to be of little help. The presence of inflamed tonsils covered with a membrane, generally unilateral, the early development of symptoms of croup, a nasal discharge—especially if abundant or tinged with blood—and a rapid enlargement of the lymph-nodes, all are strongly suggestive of diphtheria. The gradual extension of the membrane from the tonsils to the walls of the pharynx, the faucial pillars and the uvula, is diagnostic. The same is true of patches on the tonsils followed by symptoms of croup. A primary membranous laryngitis may always be regarded as diphtheria.

Bacteriological Diagnosis.—In taking a culture from the throat the swab should be rubbed firmly over the surface of the membrane and then over the surface of the culture-medium, with care not to break the surface of the medium. Some laboratories provide vials of media and swabs for

separate cultures of the nose and throat. Outfits and a skilled diagnosis are available from public health laboratories to the physicians in nearly all localities. The cultures are incubated for twelve hours, and the report is available the day following. Sometimes an immediate diagnosis may be made from the smear. With careful technic the organisms will invariably be found, unless a strong antiseptic has been used just before taking the culture. An early culture may be negative in laryngeal cases without pharyngeal exudate. Cultures in late cases may be negative unless obtained from the tonsillar crypts.

The presence of diphtheria bacilli in the throats of healthy persons does not mean the presence of diphtheria, since the carrier state is well recognized, but the combination of the microörganisms and symptoms constitutes the diagnosis of diphtheria.

Differential Diagnosis.—*Follicular tonsillitis,* which may readily be confused with the milder forms of diphtheria, as a rule is more sudden in its onset. There is usually no membrane, but there are yellowish-white, discrete deposits on both tonsils which can be removed with a swab without leaving a raw surface. In many cases a bacteriological examination is necessary for the positive differentiation.

In *Vincent's angina* the lesions develop more slowly, are usually confined to one tonsil or to one side of the throat and are more definitely ulcerative than those of diphtheria. The presence of characteristic spirilla and fusiform bacilli in the smears establishes the diagnosis.

Spasmodic croup in young children presents some difficulties. In this the obstruction usually occurs at night, comes on abruptly, is paroxysmal throughout and yields readily to sedatives and hypnotics. The voice is hoarse but not lost and there is complete relief during the intervals. There is rarely any elevation in temperature.

Scarlet fever sometimes shows a membranous pharyngitis, and diphtheria is sometimes accompanied by an erythema. It is not uncommon to find both diseases in the same patient. In diphtheria the exanthem is transient, not widespread and not accompanied by the strawberry tongue. The membrane in scarlet fever is not so thick or well-organized as that characteristic of scarlet fever. The Dick test and skin blanching test, details of which are given in the section on scarlet fever, confirm the diagnosis of scarlet fever.

Syphilitic lesions in the throat are accompanied by other symptoms, and a positive Wassermann reaction makes the diagnosis certain.

PROGNOSIS

Of the various factors to be considered in the prognosis of a case of diphtheria the two most important are the age of the patient and the prompt-

ness with which antitoxin is administered. Other factors are the previous condition of the patient, the rapidity with which the membrane is extending, the evidence of diphtheritic toxemia, the presence of complications and the individual power of resistance.

Deacon's study shows a death rate of 61.9 per cent in children under one year of age. His fatality rate is reduced to 34.7 per cent for the one-year group and to 21.4 per cent for the two-year group. The highest single year for all deaths was the third.

Delay in the administration of antitoxin increases the gravity of the prognosis.

TABLE XXII.—MORTALITY FROM DIPHTHERIA AS INFLUENCED BY ADMINISTRATION OF ANTITOXIN *

Day of Illness	Patients	Deaths	Percentage of Mortality
First †	329	5	1.52
Second	2,269	77	3.39
Third	2,407	165	6.85
Fourth	1,612	176	10.91
Fifth	911	136	14.92
Sixth	416	54	12.98
Seventh	320	53	16.56
Later	327	50	15.29
TOTAL	8,591	716	8.33

* From Kerr, *Infectious Diseases*.
† In nearly all the fatal cases attributed to the first day it is extremely probable that the duration of the disease was much longer than was alleged.

Certain unfavorable features influence the prognosis. Generally speaking, the amount of the membrane and the structures involved give a clew, but grave complications may follow comparatively mild cases. Extension of the membrane into the nasal or postnasal spaces or down into the larynx is unfavorable. Hemorrhage, either as oozing from the nose or as free epistaxis, is of grave import. Bradycardia is an ominous symptom. Marked glandular swelling is an evidence of severe toxemia. Laryngeal cases have the highest death rate. Children under three years who require intubation do poorly. Bronchopneumonia is responsible for the death of many of these cases. Late vomiting and a weak, irregular pulse are often terminal symptoms.

Paralysis may develop late in the disease, but the prognosis for ultimate recovery is favorable unless this affects a vital organ. Prognosis must be guarded, in as much as cardiac or respiratory paralysis may intervene at any time.

In general, death may be due to general toxemia, to sudden heart-failure, to asphyxia, to bronchopneumonia or to paralysis. The mortality varies in the different epidemics.

TREATMENT

Antitoxin.—The *sine qua non* of treatment of diphtheria is the early administration of antitoxin. It cannot be repeated too often that every case that is suggestive clinically of diphtheria should be treated as a positive case without the delay attendant upon a bacteriological diagnosis. Furthermore, the first dose of antitoxin should be large enough to be effective so that a repetition will not be necessary. The following dosage recommended by Park and based upon his extensive experience in the Willard Parker Hospital serves as a guide:

TABLE XXIII.—AMOUNT OF ANTITOXIN REQUIRED IN THE TREATMENT OF A CASE

PATIENTS	UNITS OF ANTITOXIN			
	Mild Cases	Moderate Cases	Severe Cases	Malignant Cases
Infants, 10-30 pounds in weight (under 2 years of age)	2,000-3,000	3,000- 5,000	6,000-10,000	8,000-10,000
Children, 30-90 pounds in weight (under 15 years of age)	3,000-4,000	4,000-10,000	10,000-15,000	15,000-20,000
Adults, 90 pounds and over in weight	3,000-5,000	5,000-10,000	15,000-20,000	20,000-30,000

* When given intravenously one-half the amounts stated.

Moderate cases that are still active and seen later than the second day of the disease, cases of laryngeal diphtheria, and those occurring as complications of the exanthemata should be treated as severe cases, with a correspondingly larger dosage of the antitoxin.

Method of Administration.—The three methods of introduction of antitoxin are subcutaneous, intramuscular and intravenous. The advantages of the intramuscular method are that the absorption is more rapid than in the subcutaneous injection, while as compared with the intravenous method it is much simpler and there is practically no danger from anaphylactic shock. Antitoxin may be given subcutaneously in mild cases in the loose connective tissue of the abdomen where the absorption is comparatively rapid. When given intramuscularly the gluteal region gives as little pain and inconvenience as any site. The antitoxin should be at body temperature and the skin prepared by cleansing and painting with iodin.

In a severe case where immediate neutralization of the toxin is imperative the intravenous method must be used. The possibility of anaphylaxis must be kept in mind. In a young child with urgent symptoms and without a history of previous injections this can be disregarded and the dose given at once. Inject 0.1 c.c. intravenously, and if no reaction occurs the whole dose may be given very slowly with careful observation of the child's con-

dition. If symptoms of shock appear, stop the injection immediately and give the rest of the dose intramuscularly.

Older children with a history of asthma or of previous injections and adults should be tested by the subcutaneous injection of 0.1 c.c. of the antitoxin. If a severe reaction occurs, desensitization is necessary, which is accomplished by repeating the subcutaneous dosage at fifteen-minute intervals until 0.5 c.c. have been given. Then give 0.1 c.c. intravenously and if no untoward symptoms appear within fifteen minutes follow with the whole dose. If there are symptoms of shock with the first intravenous dose, the small intravenous doses should be continued until the desensitization is complete.

In children with the fontanel still open the antitoxin can be injected very easily into the longitudinal sinus. In children of two years or older the median basilic vein can usually be located without undue difficulty. For the group of children in between, the external jugular vein can be used. For this the child should be "mummied" and the head turned to one side and depressed by the nurse. The crying of the child causes the vein to swell. The needle is inserted along the course of the vein toward the peripheral circulation.

For the rare cases of shock, adrenalin in 1:1,000 dilution should be administered at once in full dosage (5 to 10 milliliters).

Local Treatment.—An ice-collar worn continuously while the cervical glands are much swollen is a comfort to the patient, provided that it is well fitting.

Throat irrigations of hot soda bicarbonate solution aid in keeping the throat clear, and mechanically remove the loosening pieces of membrane. These should be given from a fountain syringe *with a rounded glass tip,* very gently. The child quickly learns to hold its head on one side with its mouth open to allow the solution to flow in and out. Any procedure that provokes resistance and struggling on the part of the child does more harm than good.

General Treatment.—The sick room should be well ventilated and the temperature maintained at about 68° F. In laryngeal cases it is desirable to have the atmosphere moist. This can be accomplished by generating steam either in a croup kettle or an ordinary kettle. Absolute rest must be enforced. Even mild cases should be confined to the bed for at least three weeks, and if there are signs of paralysis or cardiac failure this should be continued longer.

Apart from the use of antitoxin the internal treatment is purely symptomatic. Cardiac stimulants may be required to combat circulatory failure, and small doses of morphin are sometimes needed to secure rest. The

bowels must be kept open by laxatives and enemata. Dehydration must be combated by proctoclysis or hypodermoclysis.

Diet.—The diet should be bland but nourishing. The supply of liquids must be kept up. Babies on breast feeding may be fed the expressed breast milk with a medicine dropper or Breck feeder. Babies on a formula may continue their regular formula, feeding oftener and smaller amounts if the child does not take the whole amount well. If sufficient food cannot be swallowed, gavage and rectal feeding offer possibilities. For older children milk, junket, ice cream, soft-boiled eggs, gelatin, gruels and fruit juices are useful. The caloric value of any of these may be increased by the addition of lactose without altering the taste. An abundance of cool water should be taken in twenty-four hours by frequently urging the child to take a few swallows.

Intubation is indicated in laryngeal diphtheria when the respiratory embarrassment becomes so great that there is retraction of the episternal notch and the supraclavicular regions with each respiration and a pulse that disappears with inspiration. One should not wait for the exhaustion and failing circulation evidenced by cyanosis before intubation. Every community needs one physician who possesses the O'Dwyer intubation set and the ability to use it. The assistant wraps the child firmly in a confining sheet, then holds the child with the head over the edge of the table in a position to throw the trachea into a straight line with the mouth cavity. A mouth gag is inserted. The operator, with a tube of proper size for the age of the child and with a silk string firmly attached, stands at the right of the patient. With his left forefinger he locates the epiglottis. With the intubator in his right hand, the string secured around his finger, and his thumb on the releasing knob he advances the tube along the midline of the tongue until the epiglottis is reached. As the tube enters the larynx, indicated by the whistling sound, he gently raises the handle of the intubator and inserts the tube into the larynx. The tube is held in place by the left forefinger, while the obturator is gently withdrawn. The silk thread is fastened securely to the child's cheek with adhesive plaster. Many times the tube is immediately coughed out, followed by a cast of the larynx and free respiration. If it is coughed up and dyspnea returns it must be repeated.

The intubated child calls for careful watching and is best treated immediately as a case of pneumonia. A tent over the crib, and benzoin inhalations are wise measures. Often the child, terrified by the whole procedure, will not rest well until petted and soothed by the nurse. Swallowing, particularly of liquids, is attended with great difficulty. Thick cereals and ice cream are swallowed more easily. A good way is to lay the child across the nurse's lap with the head lower than the body, and feed with a spoon.

The procedure for extubation is much the same as for intubation and

should be done as soon as the fever subsides. The successful manipulation depends upon keeping the instruments parallel with the midline of the tongue.

Tracheotomy is an emergency procedure when intubation fails. As ether is contra-indicated it must be performed under local anesthesia.

Complications.—*Circulatory Failure.*—This dreaded complication of diphtheria should be guarded against by keeping the patient in bed for three weeks, even in mild cases. Cases that have been severely toxic must be protected from all physical exertion, from disturbing treatments, and kept in a recumbent position with only a low pillow until convalescence is thoroughly established. The pulse must be watched constantly, as a sudden change in the rate is often the first warning of cardiac involvement. The condition is always serious, and death threatens when there is the disturbance of violent vomiting.

The treatment is absolute rest, which is best induced by appropriate doses of morphin by hypodermic every four hours as needed: $\frac{1}{48}$ grain for a child of two years, $\frac{1}{24}$ to $\frac{1}{16}$ grain for a child of six years, and $\frac{1}{8}$ grain for a child of twelve years. Strychnin and caffein are useful as cardiac stimulants. Enteroclysis of normal saline solution at a temperature of 110° to 115° F. is of use in combating collapse and shock.

Paralysis.—This occurs about two weeks after the onset and fortunately is of short duration, hence the treatment is directed toward tiding the patient over the critical period. If the paralysis is of the soft palate or the pharynx, swallowing is difficult or impossible, and feeding should be by gavage. Paralysis of the respiratory muscles, either the intercostals or the diaphragm, interferes with respiration and with the expulsion of secretions. The patient must be kept in a position to breathe easily, and heavy bedding avoided. Secretions may be swabbed out with cotton on a dressing forceps or other applicator. Artificial respiration may be necessary. It is worth while, as the paralysis is transient. Paralysis of the oculomotor and facial nerves and those of the extremities calls for no special treatment except to protect from injury. Strychnin is the rational drug to exhibit.

Other complications call for symptomatic treatment.

Nursing.—The *nursing* of diphtheria calls for the same precautions that hold for the nursing of infectious diseases in general, with special emphasis upon the danger to the nurse herself. The nurse should be sure of her own immunity, or if in doubt should have an immunizing dose of 1,000 units of antitoxin. Greatest vigilance is necessary to avoid contact with the secretions from the nose and throat of the patient. The nurse must remember that it is possible for her to harbor virulent bacilli in her throat that are a menace to others, even though she is herself immune. If she wishes to use

a throat spray it should be very mild, as an irritated mucous membrane is easily infected. In caring for an unruly child it may be desirable to wear a mask while giving treatments. Thorough washing of the hands, followed by alcohol and a hand lotion, renders them safe.

Convalescence.—Convalescence should be carefully guarded, as paralysis occurs during the second to third week. If there are no contra-indications the child may be allowed up after the twenty-first day. The diet, which was liquid during the height of the fever, is gradually changed to a full diet for the age of the child. After convalescence is established it is very desirable for the child to have the benefit of direct sunlight a part of every day. Anemia, which is an almost constant sequel, may be treated by iron tonics, but for babies and young children the tonic of choice is cod-liver oil in full doses.

Release from Quarantine.—The New York State regulation, which may be taken as typical, allows the release of a patient from quarantine after two successive negative cultures, the cultures taken at intervals of at least twenty-four hours, and the first one taken not less than nine days from the onset of the disease. It frequently happens that negative cultures are not obtained until three, four or five weeks after the onset. In stubborn cases a virulence test may be requested from the public health laboratory.

The variety of treatments proposed for ridding a throat of persistent organisms is testimony of the unsatisfactory status of treatment. Local applications of various kinds are advocated, but are usually disappointing in their results. Some good results have been reported from the use of Roentgen ray therapy. In cases with diseased tonsils and adenoids or other abnormalities the surgical correction of these conditions is the only one that offers a reasonable expectation of relief. The presence of the diphtheria bacilli is not a contra-indication to operation.

PREVENTION

Diphtheria is unique among the contagious diseases in that there are methods, both of prevention and of cure, of demonstrated effectiveness. The ultimate aim, therefore, of the best medical practice is the eradication of the disease. The decline in the death rate in the last decade has not kept pace with the decline in the decade previous to the last. This points out clearly that greater efforts at prevention are necessary. The survey conducted by the American Medical Association considers the outlook encouraging, since in 1924 only five cities of 100,000 inhabitants and over had a diphtheria mortality greater than 20, as contrasted with 17 in the preceding four-year average; and thirty-seven cities had rates less than 10, as contrasted with 16 in 1920-1923.

TABLE XXIV.—NUMBER OF CITIES WITH VARIOUS DIPHTHERIA DEATH RATES

Years	40 and Over	20 and Over	10 and Over	Under 10
1890-1894	49	49	51	2
1895-1899	32	48	55	0
1900-1904	18	42	54	1
1905-1909	2	35	54	3
1910-1914	1	33	51	13
1915-1919	0	22	50	18
1920-1923	0	17	52	16
1924	0	5	32	37

A detailed study from the New York State Department of Health, 1912-1922, shows little decline in the death rate for the state.

TABLE XXV.—DIPHTHERIA DEATHS AND DEATH RATES PER 100,000 POPULATION IN NEW YORK STATE FROM 1912 TO 1922

YEAR	DEATHS			DEATH RATE		
	Total State	New York City	Rest of State	Total State	New York City	Rest of State
1912	1,624	1,126	498	17.2	22.7	11.1
1913	1,853	1,334	519	19.3	26.4	11.4
1914	2,015	1,492	523	20.7	29.0	11.3
1915	1,770	1,278	492	17.9	24.5	10.5
1916	1,524	1,031	493	15.2	19.4	10.5
1917	1,755	1,158	597	17.3	21.4	12.6
1918	1,776	1,245	531	17.4	22.7	11.2
1919	2,055	1,239	816	19.9	22.2	17.2
1920	1,904	1,045	859	18.2	18.4	18.0
1921	1,702	891	811	16.1	15.5	16.9
1922	1,449	870	579	13.6	14.9	12.0

The Medical Society of the State of New York, the New York State Department of Health in conjunction with the State Charities Aid Association have launched a campaign in that state to eliminate diphtheria. The slogan adopted is "No diphtheria in New York State by 1930." The physicians of the state have endorsed the plan and the district and local health officers have included it in their routine work. The support of the lay organization interested in public health work was necessary and through it the necessary funds were provided. A great deal of excellent publicity material has been widely circulated. The Metropolitan Life Insurance Company joined the campaign and are instructing their policyholders to see that every child in their family has been inoculated with toxin-antitoxin.

The following circular, issued by the New York State Department of Health, is an excellent example of the literature which is prepared for the education and enlightenment of the public:

Why Parents Should Have Their Children Protected against Diphtheria by Toxin-Antitoxin

Many parents do not worry much about diphtheria. They have read or heard about the treatment of the disease with antitoxin. They feel that with such a wonderful remedy there is little to fear.

It is true that antitoxin is a wonderful remedy for diphtheria. A few years ago, however, a method of prevention was discovered, which possibly is even more remarkable than the remedy. It was found that a child can be protected against diphtheria for several years, probably for life, by injecting under the skin a substance known as toxin-antitoxin, commonly called "T-A." T-A causes the body to form its own antitoxin so that after several months there is enough of it to successfully overcome the toxin or poison of the diphtheria germ. Furthermore there is ground for belief that once the body has formed its own antitoxin, it will continue to do so throughout life.

There are several reasons why it is better to prevent diphtheria than to depend merely upon proper treatment:

1. Antitoxin may be administered too late and in insufficient quantity to save life. Evidence of diphtheria may be so slight that a physician is not called early enough.

2. One form of diphtheria (laryngeal) attacks the larynx or wind-pipe and may cause croup but no sore throat. The child may choke to death before medical attendance can be had.

3. Another form, nasal diphtheria, attacks the lining of the nose, and may be regarded as a common cold until it is too late.

4. A person who has diphtheria must undergo a period of illness and may suffer from bad after-effects, especially heart disease.

5. Other members of the family must usually suffer inconvenience from quarantine regulations.

The Use of T-A

Hundreds of thousands of children have already been treated with T-A. It has proved itself safe. When given to young children it seldom causes disagreeable effects, except a slight temporary soreness of the arm. Older children, besides having a slight soreness where the T-A is injected, may feel a little indisposed for a day or two,—about the same as if they were "coming down with a cold."

Only three injections a week apart are usually necessary. The protection given by these injections develops slowly. It may take a few months before it is complete.

The Schick test is used only for the purpose of finding out whether or not a person is protected against diphtheria. It gives no protection and since experience has shown that the vast majority of children are not protected naturally, its general *use* is being abandoned.

The best time to have children protected by T-A is at the age of six months. Before this age the baby usually has some immunity which has been handed down by its mother.

Where the use of T-A has been systematically promoted, diphtheria has steadily decreased. Many children's institutions have been entirely freed from the disease.

In Auburn, N. Y., population approximately 35,000, where intensive work has been carried on under the direction of the State Department of Health, diphtheria has been practically eliminated. In that city there had been an average of eleven deaths a year during the eight years 1915-1922. In March of the latter year an aggressive campaign for immunization by T-A was begun. Now that sufficient time has elapsed for most of those who have been injected to form their own antitoxin, the results of this campaign leave no doubt but that diphtheria can be completely wiped out of any community. Since January, 1923—ten months after the first children were injected——there have been but four deaths from diphtheria, three in 1923 and one in (March) 1924. *There has not been a single death from diphtheria in Auburn in over twenty-eight months.*

See your physician about T-A injections for your child. He can obtain T-A free from the State Department of Health.

The toxin of diphtheria is extremely irritant and poisonous. In preparing antitoxin from horses the animals are at first subjected to a very small dose which is slowly increased and it is over two months before any appreciable amount of antitoxin can be detected in the blood. It was discovered that the addition of enough antitoxin to neutralize the toxin would result in a mixture that was only slightly toxic but was actively immunizing. This mixture is known as "toxin-antitoxin." Park standardized the dose which is now in general use in this country. It contains enough toxin to kill four guinea-pigs and to it enough antitoxin is added to so neutralize it that the whole injection would only cause slow death or paralysis to one guinea-pig. Another preparation that is widely used in France is called "toxoid." The diphtheria toxin in this mixture is treated with iodin or formalin which destroys its toxic action but does not change its ability to stimulate the production of antitoxin and promote immunity. The advantages of toxoid lie in the fact that there is no serum that may cause anaphylaxis in susceptible cases and that only two doses are necessary.

It clearly becomes the responsibility of every physician to increase his efforts in this campaign both by urging the immunization of the younger children in his clientele and adding the weight of his approval to the campaigns carried on by the school and health authorities. The immunization of school children which was first undertaken in large cities has proved to be equally applicable to small cities and is rapidly becoming a part of the school health program. This work, which was begun by Park and Zingher in 1913, has been conclusively demonstrated to be harmless and effective. The school campaigns are extremely valuable as demonstrations of the value of immunization, and through them a demand should be created for the protection of the younger children in the family so that in time all children

shall be immune before entering school. This is the only effective way of controlling the disease, since more than half of the deaths occur in the pre-school children.

Toxin-Antitoxin Immunization.—As early as 1895 several investigators, working independently, showed that mixtures of toxin-antitoxin either slightly overneutralized or underneutralized produced an immunity to diphtheria when injected into animals. The first application of this principle to humans was made by Behring in 1913, and the same year Park and Zingher began their extensive immunization of children. They did extensive investigation as to the best preparation to use, and the size of the dose. They found that a mixture that is slightly toxic to guinea-pigs and practically non-toxic to infants is effective and harmless. Three injections at weekly intervals will establish an immunity in 90 per cent of cases at the end of three months. A second series of injections will immunize 80 per cent of those left non-immune. The immunity, which depends upon the natural production of antitoxin, develops fully by the end of three months.

Method of Immunization.—The toxin-antitoxin employed for immunization is furnished without charge to physicians by the various city and state departments of health with detailed directions for its use. The injection is made subcutaneously near the insertion of the deltoid. The skin is prepared by painting with iodin, after which one cubic centimeter of antitoxin is injected. This is repeated the two following weeks in alternate arms. A sterile syringe and a needle a little larger than the ordinary hypodermic needle (a No. 23 is satisfactory) are all that is necessary.

In children under five years of age, and particularly in infants, there is practically no reaction following the injection of the toxin-antitoxin. In older children there is occasionally a reaction severe enough to keep the child out of school for a day. Any reaction that occurs is due to the protein contained in the media used in the preparation of the antitoxin. Adults sometimes give a reaction comparable to the severe reactions seen following antityphoid inoculations.

Children under six months are protected by an inherited immunity which is not rendered permanent by the administration of toxin-antitoxin. The ideal is the completion of immunization for every child by the time it reaches its first birthday. One should emphasize the fact that the younger the child the less the reaction to toxin-antitoxin and the more fatal is diphtheria. Since practically all children are susceptible under five years of age, and since the administration of toxin-antitoxin is accompanied by no ill results in young children, it is becoming the common usage to immunize preschool children and school children up to ten years of age without a preliminary Schick test. This avoids delay, unnecessary expense and the possibility of error.

The immunity from toxin-antitoxin is built up gradually and is not to be expected until from three to six months after the injection, and even then about 15 per cent may be found to be non-immune. A second series of injections in these children usually develops an immunity.

The *duration of immunity* produced in this way is of great practical importance. Park, whose records extend over the longest time, reports that children who were immunized from seven to nine years ago and have been retested yearly show almost no change from year to year. It seems safe to consider that once a natural immunity is established it becomes permanent.

The Schick Test.—*Technic.*—The dose of toxin as advocated by Schick is $\frac{1}{40}$ of the amount that would kill a guinea-pig weighing 250 grams, in 0.2 c.c. of salt solution, or $\frac{1}{50}$ of a fatal dose in 0.1 c.c. A fresh dilution of the toxin should be used for each day's work, as it deteriorates rapidly and if used errors may creep in that are most confusing. The technic is simple but it must be carried out in every detail with the greatest care. The amount introduced at each injection (0.1 c.c. or 0.2 c.c.) must be carefully measured. Outfits containing the toxin and materials for preparing the injections can be obtained from commercial houses or the state and local departments of health. Full directions accompany such outfits and they must be followed in every detail.

The test must be made *intracutaneously*. The flexor surfaces of the forearms are the best location for the injection. A control injection of heated toxin is given on the opposite arm. Heating destroys the toxin but not the protein and so is used in the control test. The skin is scrubbed with soap and water and then sterilized with alcohol. An accurate syringe and small, sharp needle are essential. Special "Schick" syringes can be obtained from any dealer. These are two in number, one being colored blue and marked "toxin" the other white and marked "control." This is desirable when one physician is performing the test, as it decreases the chances of confusing the two solutions. The needles are $\frac{1}{4}$ to $\frac{1}{2}$ inch long and of 26 gauge. The bevel is shorter than the ordinary hypodermic needle.

The skin of the forearm is held tightly and the point of the needle introduced in the skin and the dose administered. Properly done a white wheal appears which shows the hair-follicles very distinctly. If the fine needle penetrates the layers of the skin too deeply the fluid will escape into the deeper tissue, the toxin will be absorbed too rapidly and give the characteristic reaction. If the small, raised, whitish area develops we know that the test has been properly done. A bulletin of the New York State Department of Health contains an excellent description of the interpretation of the test.

The following types of reaction occur among any considerable number of persons where the Shick test has been properly applied:

(a) Positive
     1. Simple positive
     2. Combined positive
(b) Negative
     1. Simple negative
     2. Negative pseudo

The typical simple positive reaction begins on the second or third day as an erythema at the site of injection, which rapidly reaches an area of about half an inch in diameter. The border is usually fairly sharply defined. This erythema remains at its height for several days and gradually disappears, leaving a pigmented area, and is followed by localized desquamation.

In a simple negative reaction there is no appreciable result other than the slight point at the site of inoculation, of which there is practically no trace on the third day, unless there has been extravasation of blood into the skin.

In the negative pseudo reaction, there rapidly develops following the injection, sometimes within a few hours, an erythema which is apt to be much more extensive than the positive reaction. The depth of color is usually less than that which is seen in the positive reaction and the border is less sharply defined. This type of reaction usually disappears by the fourth day and leaves little, if any, pigmentation or desquamation. The erythema in the control area sometimes remains for one or two weeks in the older children.

In the positive combined reaction there is a pseudo reaction superimposed upon the positive. This results in a smaller, very deep red area beyond the border of which extends a considerably larger, lighter red area.

It is in the interpretation of the negative pseudo reactions and the positive combined reactions that the control test upon the opposite arm is especially helpful. Readings should not be made until the fourth day; some workers consider that better results are obtained by making readings on the fifth. If the readings are made too early, there is apt to be much confusion in distinguishing between the pseudo reactions and true positive reactions. The pseudo reaction, however, usually disappears at the end of three or four days following the injection. There is hardly need to mention that all doubtful results should be interpreted as positive so far as the administration of toxin-antitoxin is concerned. In negative tests it is also important to have in mind the possibility of a temporary immunity from recent injections of antitoxin as the result of a case of diphtheria or for prophylactic reasons.

Use of the Schick Test.—The use of the Schick test has contributed much to the knowledge of individual susceptibility to diphtheria, and is an effective check on the efficacy of immunization. Its practical application to the prevention of diphtheria is in the case of individuals over ten years of age for whom immunization is desirable. This applies to school children, to doctors and nurses and to adults who are in contact with the disease. After twenty years of age the percentage of the immunes reaches from 50 to 85 per cent (Park), so that it is desirable to know the necessity of administration of toxin-antitoxin before the procedure is adopted. This is more par-

A
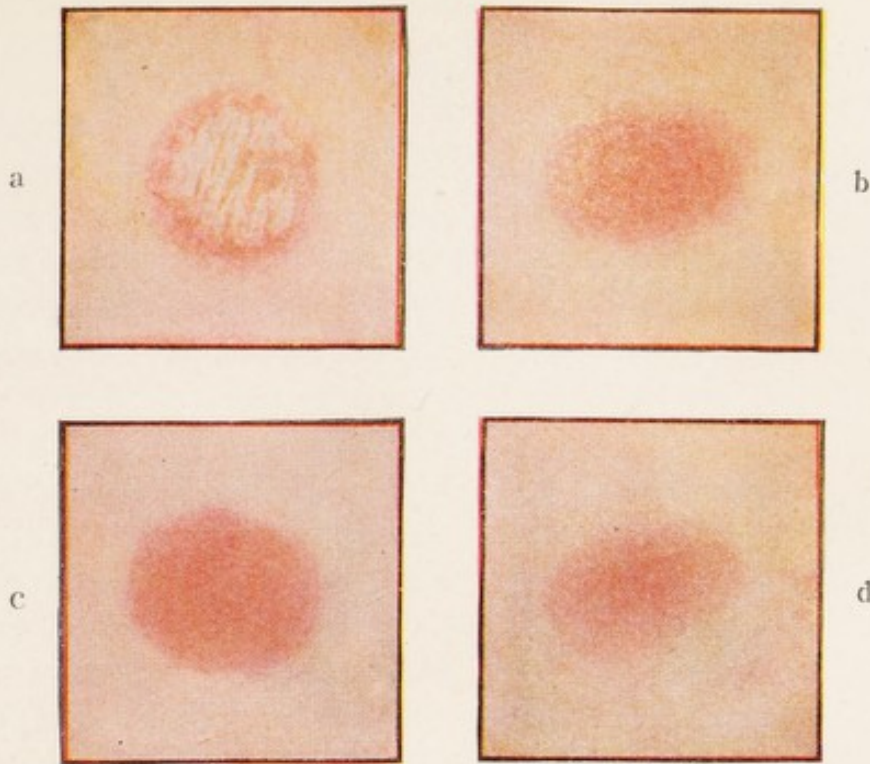
A.—Shows four typical positive Schick reactions of varying degrees of intensity forty-eight hours after test: *a* is a strongly positive reaction, with vesiculation of the surface layers of the epithelium, which is seen occasionally in individuals who have practically no antitoxin; *b* and *c* are positive reactions; *d* a moderately positive reaction.

B
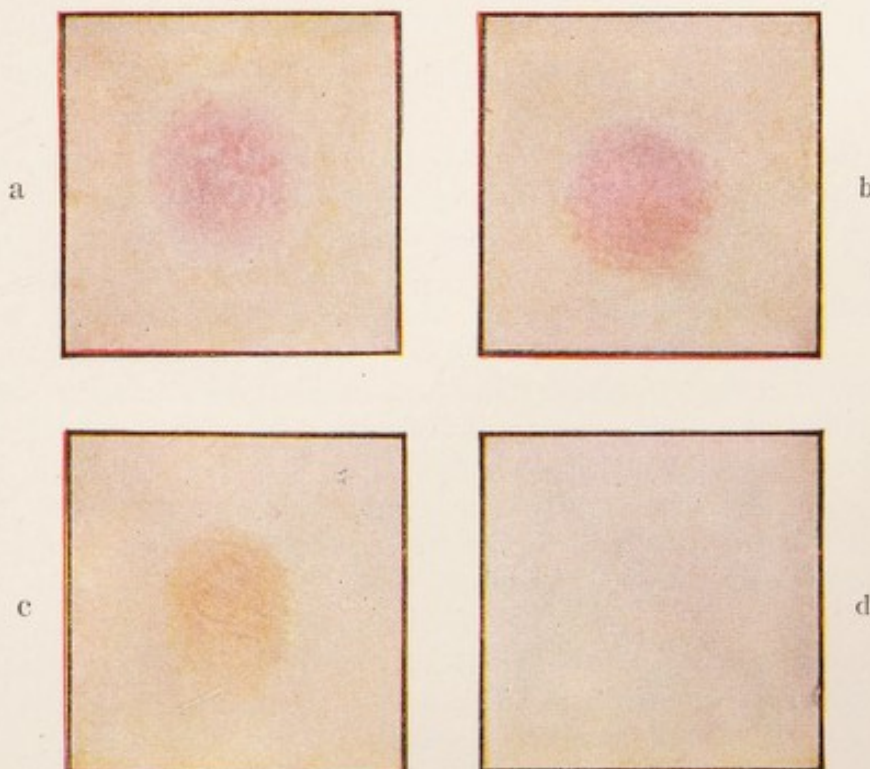
B.—Shows a fading positive Schick reaction one to four weeks after test in various stages of scaling and pigmentation; *a* shows redness, scaling and beginning pigmentation after one week; *b* and *c* pigmentation after two and three weeks; *d* faint pigmentation after four weeks.

PLATE III.—METHODS OF USING DIPHTHERITIC TOXIN IN SCHICK TEST AND CONTROLLING THE REACTION. (From *Am. J. Dis. Child.*, 1916, 11 : 269.)

ticularly true, since the reaction to toxin-antitoxin is more severe in the adult than in children.

Physicians, trained nurses and attendants who take care of diphtheria patients should submit to the very slight inconvenience of a Schick test. If a person has a negative Schick he is certain of immunity. A positive reaction would indicate the possibility of contracting the disease which could be avoided by toxin-antitoxin. There are practically no deleterious effects following the Schick test. In susceptible adults there may be quite a severe local reaction.

A retest after toxin-antitoxin checks up on the completeness of immunity. We know that from 80 to 90 per cent acquire immunity after three tests, but without a retest it would be impossible to detect the 10 to 20 per cent who did not develop complete immunity. It is valuable to retest six months after the first test. If positive, another series of injections should be given. A retest is never necessary if the first Schick test is negative.

Management of Contacts.—Each case of diphtheria is either a new focus of infection or, in the hands of an enlightened practitioner, a priceless opportunity for further work in the prevention of the disease. The plan outlined by Hitchens which is quoted below is adaptable for any community. This supplants the older method of immediate administration of antitoxin to contacts, which confers only a passive immunity of temporary duration, to be depended upon for only three, or at the most, four weeks.

1. The patient, immediately upon the establishment of probable diagnosis, will receive an adequate dose of diphtheria antitoxin and be placed in isolation. Make cultures from the seat of the disease for confirmation of the diagnosis. When the diagnosis is settled clinically or bacteriologically, or both, consider the removal of the patient to a hospital. Return to the proper health authorities whatever information may be required by local regulations.

2. Make a list of other members of the household and of probable contacts outside the domicile. Record especially their ages, and any knowledge possessed concerning their susceptibility to diphtheria. The nature and extent of this survey will depend upon circumstances; army, navy and institutional outbreaks will require obvious modifications. Gather all information possible which may lead to the identification of the source of the infection—*e.g.*, other cases, general prevalence, character of the outbreak.

3. Inspect carefully the throats of the probable contacts listed and search for any symptom of diphtheria. Those showing lesions or symptoms will be immediately treated as patients. Make cultures from the nose and throat of each member of the group and extend this survey beyond the group listed as rapidly as time and the indications permit. Isolate carriers of virulent bacilli and examine them twice each day. The first evidence indicative of diphtheria will call for an immediate therapeutic dose of antitoxin. Persons known to possess antitoxic immunity who are not carriers will require no further consideration.

4. If any of the probable contacts are so young, or are children so intractable as to make inspection of their throats a practical impossibility, and they are not known to be immune, inject them immediately with 1000 units of diphtheria antitoxin. Previous to making the injection ascertain whether or not they have ever shown symptoms of an allergic state toward any protein, and especially with regard to horses, and inject a tiny amount of the serum intracutaneously to test for intolerance to horse serum. In case hypersensitiveness is discovered withhold the serum until it is indicated for treatment; then attempt desensitization treatment. Attend all individuals injected with antitoxin as though they were patients and release them only when two negative cultures have shown that they are not carriers of virulent bacilli.

5. Make Schick tests upon all the others on the list except those known to be immune. Extend the survey of susceptibility to outside persons, making it as inclusive as conditions will permit.

6. Examine the Schick tested contacts carefully twice each day for seven days and if any one of them exhibits symptoms indicative of diphtheria, treat him immediately as a diphtheria patient (see 1 and 3).

7. At the end of from four to seven days begin the immunization, with toxin-antitoxin mixture, of all persons found susceptible. About four to six months after the third dose test them again for susceptibility.

8. As convalescence begins, release cultures from both nose and throat of patients should be made. If the carrier state is protracted, the cultures isolated should occasionally be tested for virulence; surgical interference should be called upon to aid in the elimination of virulent bacilli should they tend to persist. This may involve the removal of tonsils or adenoids or a nasal operation. The contact carriers should receive the same attention.

9. Convalescent and contact carriers should be kept in isolation until two consecutive cultures taken at about three day intervals from both nose and throat fail to reveal the presence of virulent diphtheria bacilli.

The above plan will be varied by circumstances. A milk-borne epidemic, for instance, will show definite characteristics and call for the identification of the source.

Diphtheria carriers are an important factor in the control of diphtheria. Below is quoted the position of the New York State Department of Health upon the subject:

The persistence of diphtheria bacilli for a time in the throats and noses of persons recovering from diphtheria is not unusual, and does not denote a carrier state unless the organism persists for several weeks. Carriers are not infrequently discovered who have apparently become such through contact with cases ("contact" carriers), although a searching inquiry will often reveal the fact that they have actually suffered from a mild attack of the disease. Abnormal conditions of the nose and throat appear to be largely responsible for persistence of diphtheria bacilli.

According to laboratory records approximately 95 per cent. of cultures from recovered cases and contact carriers tested for virulence up to three months from date of onset have shown virulence. In view of this fact, and since the

virulence test is one consuming several days, requests for such tests should not ordinarily be made within twelve weeks from date of onset.

In making cultures from large numbers of individuals, as in schools or institutions in which there have been no cases of diphtheria, organisms will be found in about 1 or 2 per cent. which closely resemble diphtheria bacilli, but which do not cause diphtheria or produce toxin. They can be distinguished from true diphtheria bacilli only by means of virulence tests upon animals. Cultures from carriers who are not known to have associated with a case of diphtheria *may be submitted for virulence tests immediately.*

When diphtheria is prevailing, if carriers are discovered who give no history of direct contact with a case or a carrier of diphtheria bacilli, virulence tests will be made immediately upon receipt of a detailed statement of the facts from the health officer. When a health officer feels that there are urgent reasons for requesting virulence tests upon cultures from a recovered case or contact carrier, he should take the matter up with his District State Health Officer, or with the Director of the Division of Communicable Diseases.

The control of convalescent and contact carriers is an important factor in the prevention of the spread of diphtheria. It should be borne in mind that organisms from mild cases, perhaps simulating tonsillitis, may be highly virulent for other persons.

Treatment.—The treatment recommended for diphtheria carriers is general and local in character. The general treatment consists of fresh air and exercise, sunlight, simple and nourishing diet, and painstaking habits of personal hygiene. In a majority of instances in the absence of adenoids and diseased tonsils the diphtheria bacilli will disappear without other treatment. Local applications by sprays and gargles are usually disappointing. In a series of 94 cases, 39 of whom were treated with dichloramim-T, 29 with an alkaline antiseptic spray and 26 of whom received no medical treatment, it was found that the untreated series cleared up more rapidly than either of the other two. If adenoids, diseased tonsils or other abnormalities in the nose and throat are present the condition is apt to continue until these abnormalities are removed. The presence of diphtheria organisms in the nose or throat is not a contraindication to operation. No adverse or unusual results from such operations have been reported to the State Department of Health, nor have any such been found in a survey of the literature on this subject.

With proper precautions cases may be removed to hospitals and operated upon without danger to other inmates. Such precautions consist of removal in a private vehicle accompanied by physician or nurse to see that they do not come in contact with others during the journey. After arrival at the hospital the case should be completely isolated and operated upon as promptly as possible. Isolation of the patient should continue until negative cultures have been obtained. The patient should not remain in the hospital longer than the operating surgeon deems necessary. Before taking a case to a hospital, the hospital and health authorities should be notified as to the character of the case and their consent for admission obtained.

Rules and Regulations for Control of Diphtheria Carriers.—1. A diphtheria carrier is a person who harbors in the secretions of his nose or throat the diphtheria bacillus, either following recovery from diphtheria or without himself having contracted the disease. A person who still harbors the bacilli as a result

of a recent diphtheria infection shall be regarded as a case of the disease, and not as a carrier, until at least five weeks have elapsed after the date of the first release culture. After that time the health officer may, at his discretion, regard such a person as a carrier rather than as a case.

2. The local health officer, upon the discovery of a diphtheria carrier, shall immediately advise the carrier or his guardians of the condition and give detailed instructions regarding the precautions to be observed in the disposal of the secretions of the nose and mouth and in regard to association with other persons. If the carrier is a child attending school, the health officer shall immediately notify the medical school inspector, superintendent, or principal of the school, who shall immediately exclude him from the school.

3. A diphtheria carrier shall not leave the premises upon which he resides except by permission of the health officer, who shall issue such permission only for urgent reasons and when he is assured that necessary precautions will be taken for the protection of others. But no diphtheria carrier may be granted permission to attend church, Sunday school, moving picture shows, or other places of public assemblage. He may be permitted to attend school only when, because of the existence of numerous carriers following an outbreak of diphtheria, classes are conducted in separate rooms for the diphtheria carriers, and the children who are carriers prevented from mingling with the other children.

4. Without permission from the health officer the premises occupied by a diphtheria carrier shall not be visited by children not residing there. When on such premises there are children, other than the carrier, who are attending school or Sunday school, the health officer shall immediately have cultures taken from their noses and throats for examination; and when any such children are discovered to be free of diphtheria bacilli, they are to be kept apart from the carrier and not permitted to use the same towels, eating utensils, toilet articles, etc., used by the carrier. Pending the report upon the cultures, all such children shall be excluded from school. Those children found free of diphtheria bacilli shall be returned to school if clinically free of a communicable disease.

5. No diphtheria carrier shall engage in any occupation involving the handling of milk or other food to be consumed by others, except that if a housewife, she may, at the discretion of the health officer, continue to prepare food for her family or household. Should the carrier reside or be employed upon a farm producing milk for sale, if the carrier refuses or fails to observe these regulations, the health officer must prohibit the sale of the milk, cream, butter, or cheese from such farm, except as provided in regulation 37, chapter II of the Sanitary Code.

6. When desiring a virulence test to be made the following procedure should be observed:

Take a culture in the usual way, and across the slip accompanying the culture tube request that a virulence test be made and state whether or not the patient has had diphtheria or whether he is a contact with a case of diphtheria and the date of such contact. If the virulence test upon the culture is reported by a laboratory approved for such test to be negative the restrictions on the carrier may be removed by the health officer.

7. A diphtheria carrier may be regarded as free from diphtheria bacilli and be discharged from observation and restriction when two successive cultures from the nose and throat, taken at intervals of not less than twenty-four hours,

have been found to be negative after examination in a laboratory approved for this purpose.

8. Should a diphtheria carrier be unable or unwilling to observe the precautions herein indicated, the health officer may take such further action as may be necessary to safeguard public health, pursuant to sections 25 and 326-a of the Public Health Law.

PUBLIC HEALTH REGULATIONS

In New York State all cases of diphtheria must be reported with the full name, age and address to the health officer. Cultures from the nose and throat should be submitted promptly to the laboratory of the State Department of Health or a municipal or county laboratory for the purpose of diagnosis and release. According to the New York State Sanitary Code it shall be the duty of the physician in attendance on any case suspected by him to be diphtheria to give detailed instruction to the nurse or other person in attendance in regard to the disinfection and disposal of the discharges from the nose, throat and ears of the patient. The physician or nurse or other necessary attendant upon a case of diphtheria after attendance upon the case shall take suitable precautions and practice adequate measures of cleansing and disinfection of his person and garments to prevent the conveyance to others of infective material from the patient. A case of diphtheria must be sent to a suitable hospital or be properly isolated and quarantined in the home. Such isolation to be maintained until its discontinuance is permitted by the health officer.

The minimum period of isolation is until two successive cultures taken from both the nose and throat at intervals of not less than twenty-four hours, have been examined and found negative in a laboratory approved for this purpose by the State Commissioner of Health. The first of these cultures must not be taken less than nine days from the onset of the disease. After five weeks from the date of taking the first release culture, the health officer in his discretion may declare the case to be a diphtheria carrier and subject to the special rules and regulations of the State Department of Health.

The Department of Health of the State of Illinois provides that "whenever a case of diphtheria exists in an institution, hospital, home asylum or anywhere that a group of people live under the same roof or in any other way associated closely together all contacts shall be immunized against this disease unless they have been proven to be immune to the disease by a Schick test made within three years or are otherwise known to be immune by reason of active immunization with toxin-antitoxin. Those not so immunized or known to be immune shall be quarantined or removed."

No child who has had diphtheria can return to school until recovery and two successive cultures from the nose and throat at least twenty-four hours apart contain no diphtheria bacilli. Other children of the same household if

the patient remains isolated at home cannot return to school until termination of quarantine or removal from quarantined premises and until two successive cultures from the nose and throat at least twenty-four hours apart show no diphtheria bacilli. If the patient goes to a hospital or the other children leave home when the disease is discovered they can return to school when two successive cultures from throat and nose taken after removal and at least twenty-four hours apart show no diphtheria bacilli. The same rule applies to other children or contacts who have been exposed.

The Committee of the American Public Health Association on Standard Regulations for the Control of Communicable Diseases summarizes our present knowledge of diphtheria as follows:

1. INFECTIOUS AGENT.—Diphtheria bacillus, *Corynebacterium diphtheriæ*, the Klebs-Loeffler bacillus.

2. SOURCE OF INFECTION.—Discharges from diphtheritic lesions of nose, throat, conjunctiva, vagina, and wound surfaces. Secretions from the nose and throat of carriers of the bacillus.

3. MODE OF TRANSMISSION.—Directly by personal contact, indirectly by articles freshly soiled with discharges, or through infected milk or milk products.

4. INCUBATION PERIOD.—Usually two to five days, occasionally longer if a healthy carrier stage precedes the development of clinical symptoms.

5. PERIOD OF COMMUNICABILITY.—Until virulent bacilli have disappeared from the secretions and the lesions. The persistence of the bacilli after the lesions have healed is variable. In fully three-fourths of the cases they disappear within two weeks. In 95 per cent of cases, the bacilli disappear in four weeks. In exceptional cases virulent bacilli remain in the throat and discharges for from two to six months.

6. METHODS OF CONTROL

(a) The infected individual and his environment

1. *Recognition of the Disease.*—By clinical symptoms with confirmation by bacteriological examination of discharges.

2. *Isolation.*—Until two cultures from the throat and two from the nose, taken not less than twenty-four hours apart, fail to show the presence of diphtheria bacilli. Isolation may be terminated if persistent diphtheria bacilli prove avirulent. Where termination by culture is impracticable, cases may be terminated with fair safety as a rule sixteen days after onset of the disease.

3. *Immunization.*—Exposed susceptibles who cannot be kept under daily observation by a physician or nurse should be promptly immunized by antitoxin. (By susceptibles is meant such individuals as are found to be nonimmune by the Schick test, *i.e.,* those who give a positive reaction.)

4. *Quarantine.*—All exposed persons until shown by bacteriological examination not to be carriers.

5. *Concurrent disinfection* of all articles which have been in contact with the patient and all articles soiled by discharges from the patient.

6. *Terminal Disinfection.*—At the end of the illness, thorough airing and sunning of the sick room, with cleaning or renovation.

(*b*) General measures

1. Pasteurization of milk supply.

2. Application of the Schick test to all especially exposed persons, such as nurses and physicians, and active immunization of all susceptibles, but not within three weeks after the administration of antitoxin.

3. Active immunization of all children by the end of the first year without prior Schick testing; active immunization of school children with or without prior use of the Schick test.

4. Determination of presence or absence of carriers among contacts and, so far as practicable, in the community at large.

CHAPTER XI

TYPHOID FEVER

Definition.—Typhoid fever is an acute generalized infection caused by the *Bacillus typhosus.* It is usually characterized by high fever which lasts about four weeks, and severe enteric symptoms. The latter include diarrhea, abdominal tenderness, tympanites and spleen enlargement. It may be acquired at all ages, but is more common in youth and early adult life. While it is frequently a severe and oftentimes fatal disease, cases are sometimes so mild or the symptoms so masked as to be classed merely as an ordinary gastro-intestinal disturbance. Since animals are not susceptible to the disease each case must come from a previous human case, either directly as by soiling the hands with the discharges of the patient and the subsequent transfer of the infective organisms to the mouth, or indirectly as by the infection of drinking water, milk or by foods eaten raw.

Synonyms.—Enteric fever, autumnal fever.

HISTORY

Typhoid fever is undoubtedly a disease of great antiquity, for while the disease was not known by this name until nearly the middle of the nineteenth century, there is every reason to suppose that the continued fevers of seasonal occurrence described by Hippocrates and Galen and characterized by diarrhea, abdominal pain, biliousness, vomiting and other classical symptoms of typhoid fever really were that disease.

The lesions caused by typhoid fever were described in considerable detail and very much as we now know them to be, as early as the beginning of the nineteenth century, but very little was known as to the mode of transmission of the disease until about three-quarters of a century had passed. Various theories were advanced, some decidedly fantastic, others based on the supposition that the infecting element was contained in the bodily discharges.

Thomas Willis, an English physician, described an outbreak among English troops in 1643. This is probably the first full description of the disease.

Typhoid fever was given its present name by Louis in 1829, but it was not clearly distinguished from other intestinal diseases, notably typhus fever, until 1837 when Gerhard of Philadelphia, a pupil of Louis, outlined in a

masterful manner the differences between what was then the two very common so-called filth diseases. His studies were verified by the Jacksons, father and son, Enoch Hale and George C. Shattuck of Boston and others, including Bartlett who in 1842 published a treatise which clearly differentiated the two diseases. Budd (1856) was the first to insist that human excreta were the means by which the disease was conveyed.

The organism causing the disease was not discovered until 1880. Eberth, who published the result of his investigation in July of that year, is generally given credit for this discovery, but Klebs actually made public his researches on the subject some three months earlier. In 1881 Koch followed with his description and photomicrographs of the same organism which he, working independently, had isolated.

According to Gay, to Klebs should go the credit of first suggesting the name *Bacillus typhosus* for the causative organism and for his attempt in 1881 to cultivate this bacillus outside the human body. In this experiment he prepared and sterilized gelatin culture-media and inoculated them from the mesenteric lymph-nodes of a case of typhoid fever. In 1884 Gaffky isolated the typhoid bacillus in pure culture, using solid media, and to him is usually given the full credit for first having performed this step.

During the next few years various other observers isolated the organism from different organs of the body. In 1885 Pfeiffer isolated *Bacillus typhosus* from stools, and the following year it was found by Hueppe in the urine of a typhoid case. It was in 1886 that it was discovered in the circulating blood, thus showing the disease to be a bacteriemia. With this knowledge further steps in the accurate diagnosis and control of the disease followed in rapid succession. The first suggestion that typhoid bacilli could be carried by healthy individuals or by persons presenting atypical symptoms was recognized as early as 1887. In 1896 Widal introduced his method of making a differential diagnosis known as the Widal reaction, which depends on the agglutinative property of the blood of a typhoid case or carrier of typhoid organisms in a liquid medium. The agglutinative power of the blood of a typhoid patient does not readily develop during the first week of the disease. Conradi in 1905 devised a method by which typhoid fever could be detected in the blood of a patient during the first seven days of illness. This consisted in obtaining several cubic centimeters of blood, best obtained from the median cephalic vein, mixing with about 15 c.c. of bile media and incubating.

Attempts were made as early as 1893 to immunize individuals against typhoid fever by means of subcutaneous inoculation of killed cultures of the organisms, but unfortunately this method was not developed rapidly enough for use during the Spanish-American War during which more American soldiers died from the disease than from Spanish bullets. Studies made during this war, however, brought out very clearly the fact that the excreta

of typhoid cases and carriers must be carefully disinfected, else the organisms of the disease may readily be transmitted to healthy individuals by flies, drinking water, foods, as well as directly from person to person.

In those centers of population which obtained their public water supplies from polluted sources, typhoid cases were, up to about this time, the mainstay of many a physician's practice, but with the growth in the knowledge of how typhoid fever was transmitted, sanitary engineers rapidly developed effective methods for the purification of such waters. Cities which had been repeatedly visited by epidemics of typhoid fever and which normally had a high typhoid morbidity and mortality rate found that by the application of such purification methods the incidence of the disease was rapidly reduced to a few sporadic cases. To-day the community which develops a typhoid epidemic usually becomes the object of inquiry and investigation by state health authorities.

INCIDENCE

Whether a given community will have a large or small amount of typhoid fever depends in no small measure on the purity of its water supply. If the latter is taken from a polluted source the typhoid rate will unquestionably be high, as it was in such cities as Pittsburgh, Philadelphia and Albany before steps were taken to purify the water furnished in these municipalities. Occasionally typhoid outbreaks, widespread and often explosive in their incidence, will occur in places where the water supply is pure or subjected to purification processes. In such instances the cause will usually be found to be inefficient handling of the purification process, a leaky valve on some dual water system, or a typhoid case or carrier or an infected well on a dairy farm which supplies the community with milk. Limited outbreaks may be due to infected milk from a small dairy or the ingestion of food infected by a carrier. Sometimes extensive and widespread outbreaks of typhoid fever are due to infected milk, as in the Montreal epidemic in the spring of 1927 when over five thousand cases and five hundred deaths resulted from the use of infected milk. Sporadic cases can often be traced to contact with a person ill with typhoid and the carrying of infection from such a person by flies or to a visit to a community or localities where typhoid is present. In recent years the incidence of typhoid fever has fallen to a very low figure in municipalities having efficient health departments.

Age.—Typhoid fever is a disease which attacks all ages, but it occurs most frequently in youth and early adult life, the greatest susceptibility apparently being between the ages of fifteen and twenty-five. Probably most doctors to-day will claim that there are few or no cases in children under two years of age. This is not so, however. While it appears to be relatively rare in children under five years of age, such cases are by no means unknown,

large children's hospitals frequently having a number of patients of tender age at the same time. Very young infants have been known to have the disease and the causative organism has even been isolated from the blood in the fetus and in the newborn.

In this disease there is apparently no immunity conferred by age. In very young children it is often of the benign type. While not uncommon in old age, symptoms are frequently atypical and consequently the disease is harder to diagnose. Possibly very young children are relatively free from the disease because they are less frequently exposed.

Sex.—Sex has no influence apparently on the incidence of the disease.

Season.—Typhoid fever is commonly supposed to be more prevalent in the late summer and early autumn, but it can and frequently does occur at all seasons of the year. The more relative frequency in the warmer months of the year can be explained partly by the prevalence of flies at that time, by the fact that the organism will remain viable outside the body for a longer time in warm weather, and by the greater tendency of people to make visits, excursions or long trips when weather conditions are favorable.

ETIOLOGY

Typhoid fever is caused by the *Bacillus typhosus* of Eberth. It is an actively motile organism belonging to the colon group. During the course of the disease it is found in enormous numbers in the feces and urine. It has occasionally been isolated from the sputum of a typhoid patient. The bacillus grows readily in the bile and is frequently found in the gall-bladder of carriers. This ability to grow in bile to the practical exclusion of other organisms is made use of in the laboratory as a convenient means of isolating the bacillus in pure culture from feces.

Every case of typhoid fever means that the alvine discharges of one person are taken into the digestive tract of another. This is invariably due to carelessness and uncleanliness.

Transmission may be direct, semidirect or indirect. As an example of direct infection a nurse may become infected from handling the discharges of a patient; or (semidirectly) her hands may become soiled with typhoid bacilli from infected utensils or materials recently handled by a typhoid patient or carrier. Unless the attendant is more careful and cleanly than the average it is generally not long before infected hands are put to lips or mouth or to some article of food. Thus the route is completed from the intestine of one person to the digestive tract of another. Each of these modes of transmission is responsible for many secondary cases of the disease. The third or indirect mode is usually by means of water, milk or other foods, and is generally the way that explosive and widespread outbreaks are caused.

In the case of the direct or semidirect modes there is practically no chance for the causative organisms to increase in numbers, but usually there is, on the other hand, very little opportunity for them to decrease or to attenuate or lose virulence.

In the case of water as a vehicle, great dilution occurs and quite some time may elapse between the time of passage from the bowel to the time of ingestion. Where public water supplies are involved probably large numbers of people escape for the reasons given, or because of a natural or acquired immunity, but such outbreaks are frequently scattered widely over the area supplied by that particular water system. Outbreaks due to milk and foods are usually explosive in character, for the typhoid organisms have a chance to multiply greatly in media of this kind. The number of bacilli ingested in such cases must frequently be enormous. Foods served hot are, of course, safe if thoroughly cooked, but sometimes foods are infected after they have cooled subsequent to cooking.

While the period of greatest infectivity is apparently during the second and third week of the disease, typhoid bacilli are reported to have been found in some instances in the feces and urine of cases during the incubation stage of the disease. Flies have been proved to be capable of conveying typhoid germs from excreta to food; a good argument for careful disinfection of all typhoid dejecta and the careful screening of houses.
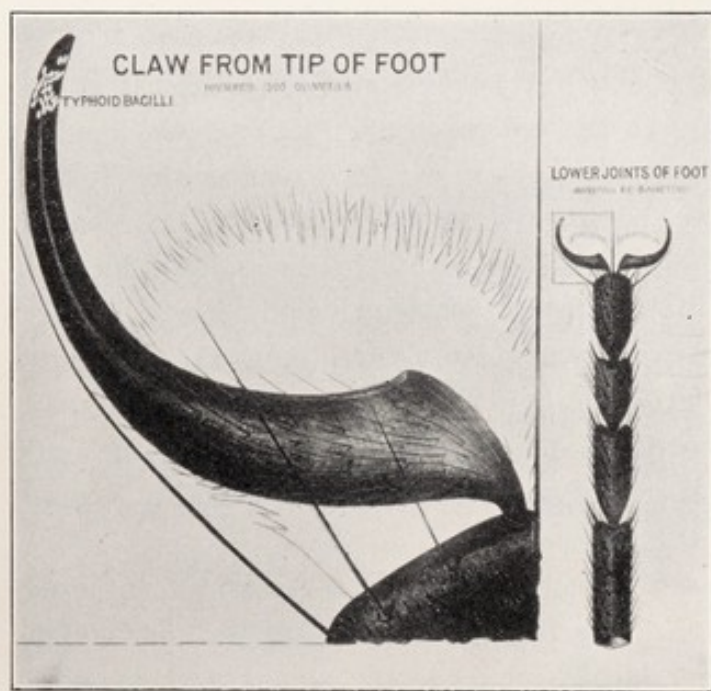
FIG. 9.—TYPHOID FEVER.
The foot of the fly, magnified, showing a frequent means of transmission.

BACTERIOLOGY

Bacillus typhosus (Eberth), the organism causing typhoid fever, is a non-spore-bearing, motile bacillus, about 1 to 3 micra in length by 5.5 to 0.8 micra in thickness, belonging to the colon bacillus group. In liquid media it may grow somewhat longer. Flagella, eight to ten in number and arranged peritrichously, may be demonstrated by proper staining.

The technic of isolating the typhoid bacillus from the blood or from urine and feces is a complicated laboratory process which can be satisfactorily performed only by those who have been thoroughly trained for this

work. Therefore, no attempt will be made in this volume to discuss these processes, which are described in detail in several of the later bacteriological manuals.

Every physician should, however, be thoroughly conversant with the method for the collection and submission of specimens of urine and feces from suspected typhoid cases and of blood for the Widal diagnostic test. Practically all laboratories equipped for work of this kind furnish outfits for the collection of such specimens accompanied by detailed directions which should be carefully followed.

Incubation Period.—The incubation period of typhoid fever is usually from one to two weeks, with the average about ten days, but it may be considerably shorter, depending to a considerable extent apparently on the massiveness of the dose of infecting material. Gay records cases infected in the laboratory which developed symptoms within two days.

PATHOLOGY

The lesions so common and characteristic of typhoid fever in adult life are modified to such an extent in childhood that a detailed statement is necessary.

Ulceration.—Only about the age of puberty and beyond are ulcerations found as commonly as in adult life, although extensive ulceration may occur as early as six years. In fetus and congenital cases intestinal ulceration has not been found and it may be missing even in older cases. Up to about six years of age some ulceration may be found, but it usually is slight and superficial.

The size and extent of an ulcer depends on the amount of the original necrosis, the sloughing proceeding from the edges inward. In separating the slough exposes the muscularis and mucosa, the former being the base of the ulcer in most cases. An entire Peyer's patch may slough. Intestinal ulcerations are frequently rounded or oval in shape, but the borders may be jagged or angular.

Healing commences with granulation at the base of the ulcer, the mucosa gradually extending and new epithelia forming. The healed ulcer is depressed and pigmented.

Hemorrhage.—In a series of cases reported by Weston and Radbill hemorrhage in children over fifteen years of age was nearly as common as in adults. Under the age, however, it appears less frequently, while below the age of ten it is practically unknown, although occasional instances have been reported. In such small children, however, it is seldom of serious moment. Bleeding seems to be the direct result of the separation of the sloughs.

Perforation.—Perforation in infancy is rare and seldom takes place under five years of age, the probability of its occurrence increasing with age. Over five it is only one-half as common as in adult life, according to Jopson and Gettings. These authors also give twenty and twenty-one months as the youngest authentic ages of its occurrence.

Typhoid fever is further characterized by swelling of the mesenteric glands and spleen, and parenchymatous changes in other organs, particularly the liver. Ulceration of the larynx occurs in some cases, the cartilages frequently becoming involved. Ulceration of the glottis may take place. Heart lesions are more common than is generally supposed.

SYMPTOMS

During the period of incubation, which is from two to three weeks, no symptoms are observed with the exception of a slight evening rise in temperature. The onset as a general rule is insidious, but in young children it is more apt to be abrupt, the first symptom noticed being a convulsion, followed by vomiting, giving every indication of meningeal irritation. Headache is nearly always present and increases in severity during the first week. The muscles are sore and tender, the face is flushed and the patient complains of chilly sensations. Nosebleed is a frequent symptom in the early stage. The bowels may be sluggish in action, but diarrhea is more frequently present. The appetite is very poor at this period and the tongue becomes furred. At this stage also the temperature chart shows a characteristic steplike ascent. Each day the morning and evening temperature is slightly higher than the preceding day. The pulse rate does not increase in proportion to the rise in temperature, but it is relatively higher in young children. The abdomen is often slightly distended and tender when palpated, this tenderness being more marked over the right inguinal region where gurgling can usually be elicited. The spleen is found to be enlarged by the end of the first week. Rose spots appear over the abdomen during the first week and may be so profuse as to resemble measles, but in children may be slight and not characteristic. The eruption may be seen on the chest and back and may appear in successive crops. It usually lasts about ten days. There is nearly always a slight bronchitis with a more or less severe cough.

The next stage is known as that of continued fever. By this time the level of the temperature is maintained, although the line is broken by morning remissions which become greater without any change in the height of the evening temperature. The eruption is at its height during this stage, which is also called the stage of eruption. The pulse remains much slower than the height of the temperature would indicate. The spleen, which feels tense and hard to touch, becomes more enlarged, its greatest enlargement being

found in this stage. The enlarged spleen is more marked in children. During this period there are apt to be a number of nervous symptoms, but they are not so severe and constant as in adults. Children are usually apathetic, dull and listless. There is frequently delirium when the fever is high, especially at night. The so-called typhoid state sometimes found in adults is not common in children. The reflexes may be increased and ankle clonus is present. Incontinence of urine and feces is common.

The third stage, or the period of defervescence, usually appears about the third week and is characterized by a falling temperature and improvement in the nervous and intestinal symptoms. The temperature curve shows an increase in the daily remissions and a gradual fall to normal, especially in the evening. The spleen softens and diminishes in size. The rash has disappeared and the appetite improves and sleep becomes more normal and refreshing.

The stage of convalescence develops gradually and with it a marked improvement in the child's condition. The temperature does not rise over 100° F. and the pulse improves in volume and strength.

These stages, which are characteristic in adult typhoid, may be absent in young children. After the age of ten years the adult features of the disease are generally present. In younger children the febrile stage may only last a week. Typhoid fever in young children is usually of a much milder form and of shorter duration. The nervous symptoms in young children may overbalance those of the intestinal tract. Loss of appetite is an early symptom. This combined with the high fever soon brings about a condition of prostration and emaciation. The loss in weight may be due to starvation. With the decline in temperature the appetite generally returns and often is voracious.

The blood in typhoid is characterized by a decrease in the number of white blood-cells. The red cells show no change outside of a slight anemia. The leukopenia is not present in the first week but appears about the tenth day. The differential count is normal with the exception in young children of a slight increase in the number of lymphocytes. Blood cultures show the presence of typhoid bacilli early in the disease but they usually disappear not later than the third week.

Tympanites is a distressing symptom and causes shortness of breath from pressure upward on the diaphragm. This condition may be associated with diarrhea. Children fed on a milk diet, according to Kerley, usually have distention and diarrhea. The tympanites is caused by an unfavorable intestinal flora, not by the *Bacillus typhosus*. Diet with a high carbohydrate and high caloric content is most beneficial in these cases.

Typhoid in Infants.—Such cases show few of the typical signs of typhoid. The rose spots may be few in number and the temperature curve
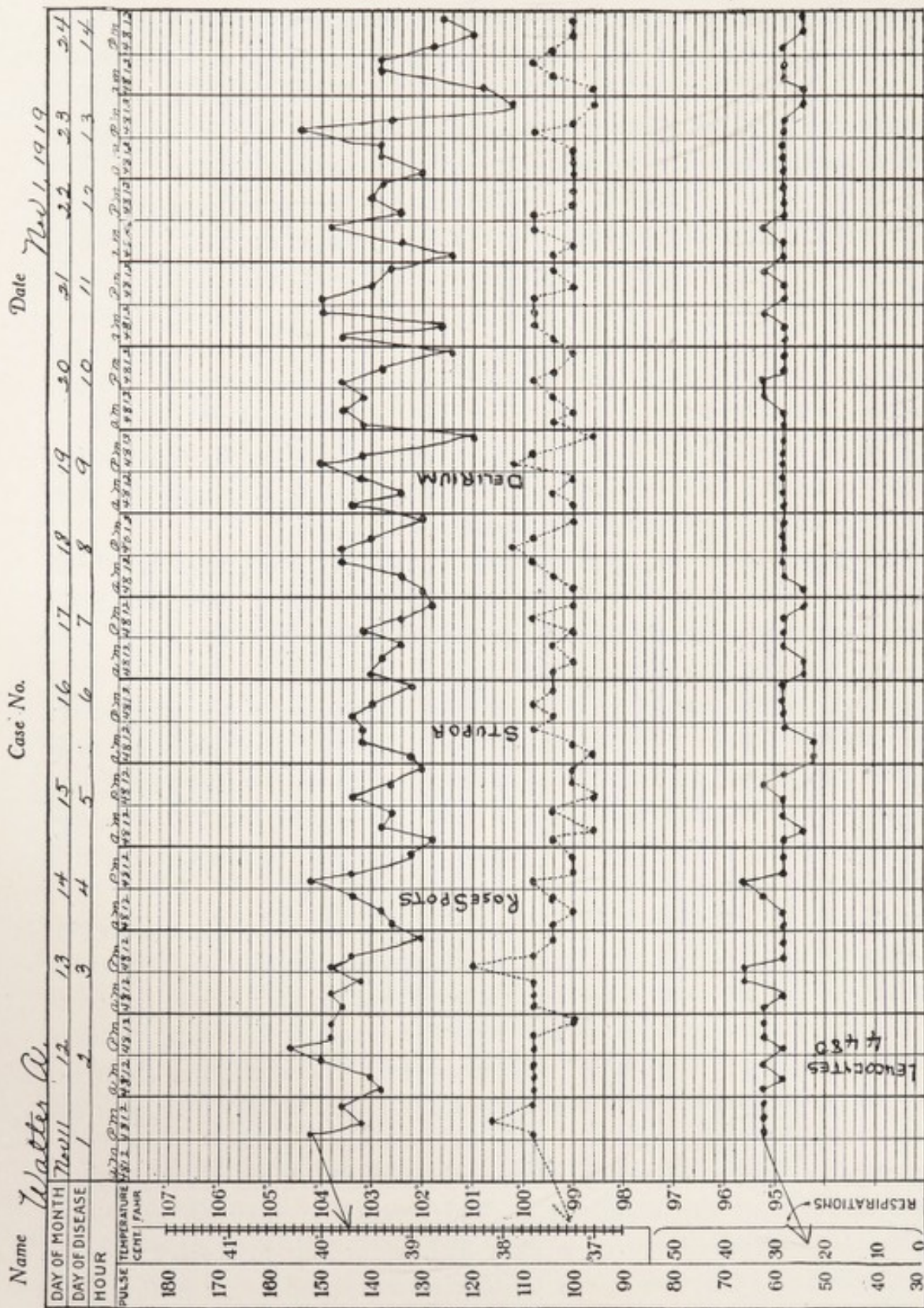
FIG. 10.—TYPHOID CHART.

Boy seven years old. Marked cerebral symptoms.

Fig. 10.—Continued.

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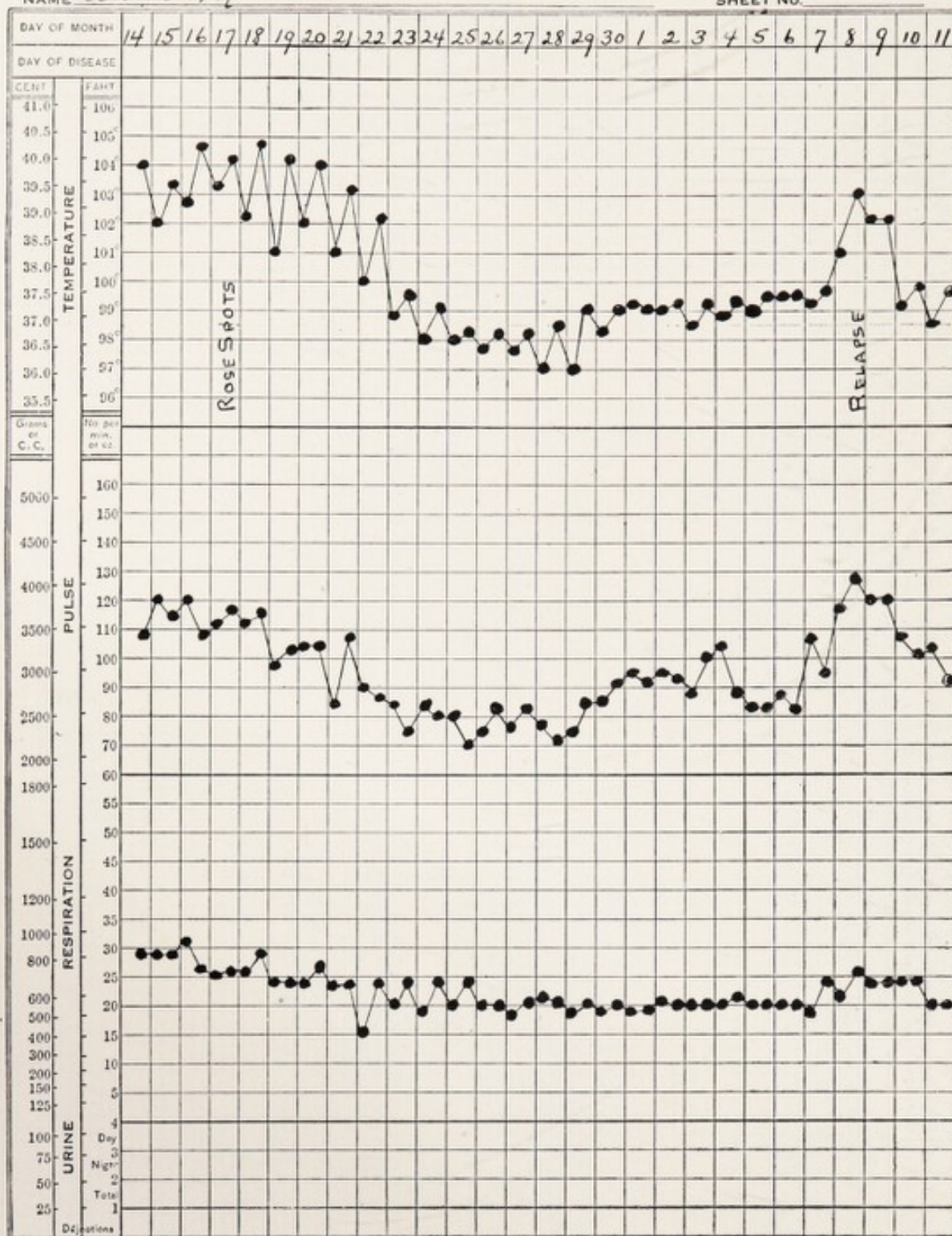
Fig. 11.—Typical Typhoid Chart.
Child eleven years old.

low and not typical. The pulse is high and irregular. Vomiting is an important and persistent symptom. The nervous symptoms are marked, especially twitching of the muscles and convulsions. The Widal test is positive.

COMPLICATIONS

These are not frequent or so severe in children as in adults. Their presence, however, is responsible for over two-thirds of the mortality of typhoid.

Intestinal hemorrhage is rare in children under ten years of age. Holt refers to a fatal case of intestinal hemorrhage in a child of four and a half years of age. Such hemorrhages are accompanied by symptoms of shock—sudden fall in temperature, rapid and small pulse, shallow respiration, cold extremities, restlessness. They occur most frequently after the second week. Intestinal perforation and peritonitis are even more rare than hemorrhage.

Bronchopneumonia is responsible for many of the fatalities of typhoid fever in infants. A slight bronchitis is present in most of the cases. Pleurisy may develop, but it is uncommon. Complications affecting the nervous system are not common. Meningitis may develop at any stage of the disease, due directly to the typhoid bacillus. Meningism sometimes is observed in children. Cases of aphasia have been reported, as have cases of acute insanity and other psychoses. The writer had a case of acute mania in a boy five years of age with typhoid which lasted six weeks. The prognosis is good in these cases. Chorea not infrequently follows typhoid fever in young children.

Small abscesses and furunculosis occur on the back of the head or body. They are due to a pyogenic coccus and not to the typhoid bacillus. Bedsores are an indication of neglect or incompetent nursing.

The bones and joints may be involved and the condition not develop for months after the fever. Children are not so apt to develop a typhoid arthritis, but osteomyelitis and periostitis of one or more bones are not unusual in these cases. A "typhoid spine" has been described which is a spondylitis due to the typhoid bacillus. Pain on motion is a prominent symptom and as a result the spine is held rigid.

Otitis media is a common complication in children, and while the typhoid bacillus has been found in the discharge, the infection is usually due to pyogenic organisms.

Relapses appear to be more frequent in early childhood than in later life. This is a secondary attack developing after a longer or shorter fever-free interval. The secondary attack is marked by a reappearance of the temperature curve and many of the original symptoms, including the rose spots and enlarged spleen. They last from two to three weeks and are more marked

after mild attacks of typhoid. The typhoid bacilli renew their attack on the lymphatic tissues after the body tissues seem to lose the immunity acquired by the first invasion.

DIFFERENTIAL DIAGNOSIS

Paratyphoid is similar in many respects to typhoid, but due to different organisms called paratyphoid "A" and paratyphoid "B." It can only be differentiated by bacteriological examination. The Widal reaction is the most important positive means of diagnosis. It is present after the seventh day in over 90 per cent of cases. The temperature curve, low white blood-cell count, slow and irregular pulse, skin eruption, enlarged spleen and intestinal and nervous symptoms indicate typhoid. These clinical symptoms are often atypical in young children and one would hesitate to make a diagnosis of typhoid from clinical signs alone unless in the presence of an epidemic.

For the Widal test a small quantity of blood may be taken from the lobe of the child's ear or the finger tip or heel in young children, and sent to the nearest laboratory equipped to do this work. Some laboratories have outfits for collecting the dried blood, others furnish capillary tubes which are sealed after collecting the blood by heating the tip of the tube in a flame so the blood reaches the laboratory in liquid form. Specimens of feces and urine should be obtained and sent to the laboratory for the detection of the typhoid organism. Such examinations are essential in order to determine whether there are persons who are carriers in outbreaks where no early active cases are to be found.

Typhoid in children may be confused with several other infections. *Acute miliary tuberculosis* may resemble typhoid. The failure of the Widal reaction, the absence of typhoid bacilli in the stools and a positive Pirquet skin tuberculin reaction would exclude typhoid.

Ileocolitis presents more severe intestinal symptoms and diarrhea than in typhoid, the temperature does not rise in a characteristic manner, leukocytosis is usually present and there are no rose spots, eruption or positive Widal.

Septic conditions arising from various infections may be confused with typhoid fever. Among such conditions may be mentioned septic endocarditis, pyelitis, osteomyelitis, and general septicemia. Persistent negative Widal tests, leukocytosis, rapid pulse, blood cultures showing organisms other than the typhoid bacillus, and the appearance of localized symptoms should clarify the diagnosis.

Meningitis in the early stages may resemble typhoid in children, especially when the symptoms show meningeal irritation. The examination of the spinal fluid after lumbar puncture should be made without delay in all

such cases. Otherwise a positive diagnosis of typhoid cannot be made until the Widal reaction can be obtained or the characteristic symptoms appear.

Epidemic encephalitis may bear a close resemblance to typhoid. The onset in both is generally gradual and the temperature in both may be high. Evidences of meningeal irritation often occur in typhoid in children. Lumbar puncture may be negative in both diseases. The blood in encephalitis shows an increase in the leukocytes and in the polymorphonuclear cells. It never shows the specific agglutination reactions. The enlarged spleen, rose spots and slow pulse are absent in epidemic encephalitis.

Malaria may be differentiated by finding the malarial organism in the blood smears.

PROGNOSIS

In general the prognosis of typhoid fever in children is favorable, more so than in adult life. In early infancy, on the other hand, the prognosis is not so favorable. Griffiths and Ostheimer reported a group of 278 cases in infants under two and a half years in which the mortality was 57 per cent. The authors, however, state that this is not representative, as only the severe and serious cases were included. A collected series of reports of several authors of cases in children from two to twelve years of age showed a mortality ranging from 2 to 4 per cent. Holt stated that the mortality in children over three years of age does not exceed 3 or 4 per cent.

Table XXVI shows the death rate per 100,000 population in the United States registration area in comparison with rural and urban sections in New York State. An interesting fact is that the rate in the United States is over twice as high as in New York State and that prior to 1921 it was about twice as high outside of New York City as in the rest of the state.

TABLE XXVI.—Death Rate for Typhoid Fever per 100,000 Population of the United States Death Registration Area of New York State from 1915 to 1925

Year	United States Registration Area	New York State	New York City	New York State Exclusive of New York City
1915	12.4	7.8	6.4	9.4
1916	13.3	6.0	4.1	8.2
1917	13.5	5.9	4.2	7.7
1918	12.6	5.6	3.6	8.0
1919	9.2	3.6	2.2	5.3
1920	7.8	3.5	2.4	4.9
1921	9.0	3.6	2.2	5.2
1922	7.5	2.9	2.2	3.7
1923	6.8	2.9	2.4	3.4
1924		3.3	3.2	3.5
1925		3.6	3.4	3.8

TABLE XXVII.—MORTALITY FROM TYPHOID PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1922, ACCORDING TO MONTHS

Year	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1915.....	56	35	49	32	44	48	54	91	101	100	79	86
1916.....	..	..	..	..	..	..	..	..	..	..	..	..
1917.....	40	44	40	38	39	36	47	67	84	65	59	34
1918.....	28	21	34	29	44	30	50	54	77	144	31	33
1919.....	26	22	21	16	26	14	34	42	59	48	31	35
1920.....	17	12	13	30	16	20	42	49	64	51	24	33
1921.....	24	15	27	15	16	24	36	42	51	59	36	32
1922.....	21	11	20	15	20	22	23	47	32	44	30	31

TABLE XXVIII.—TYPHOID FEVER DEATH RATE PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1924, ACCORDING TO SEX

Year	Male	Female
1915	10.1	5.7
1916	7.3	4.9
1917	7.2	4.6
1918	7.0	4.3
1919	4.3	3.0
1920	4.3	2.8
1921	4.2	2.9
1922	3.5	2.4
1923	3.5	2.3
1924	3.5	2.7

Improvement of municipal water supplies, sanitary milk production, and improved sewage disposal methods account for the gradual reduction in mortality in New York State.

The influence of the time of year is shown in Table XXVII. The autumn months show the greatest mortality, probably as a result of a greater morbidity at this time of year.

The death rate by sex in New York State shows a consistently higher rate among males (Table XXVIII).

The prognosis in cases complicated by hemorrhage, high fever, delirium, tympanites, etc. is much graver. Perforation is fatal unless relieved by an early operation.

The state of nutrition has an important bearing on the child's recovery. Children who are undernourished or who refuse to take food or fluid are not so apt to make as rapid and complete a recovery as those who have a good appetite and retain and assimilate nourishment throughout the illness.

TREATMENT

Prophylaxis.—The offender in the spread of this disease is man himself. The causative agent, *Bacillus typhosus,* is a parasite in existence in the

human body and is expelled through the discharges of persons ill with the disease and also in a small proportion of cases in those who have recovered from typhoid, and who are therefore known as "carriers." With these facts in mind it would seem a relatively simple matter to control and even exterminate the disease. Human nature is difficult to control and a great proportion of the population is careless and indifferent in matters of personal and public hygiene. The bacillus, in order to cause disease, must be taken into the body through the mouth and swallowed. The contamination of public or private water supplies is the most frequent source of infection. The water used to wash milk cans and possibly to adulterate the milk makes the milk supply at times a source of danger. Cows do not have typhoid, but the dairy employees can and often do infect the milk. When the water supply is not above suspicion all water used for drinking, diluting food, washing vegetables, nursing bottles, nipples, etc., should be boiled. Boiling milk for five minutes will destroy any typhoid germs present. When away from home or traveling the mother should insist on boiling both water and milk for the child.

The control of patients is more difficult in the home than in a hospital. Isolation is unnecessary when proper attention is paid to cleanliness and disinfection. All discharges must be disinfected. The stools and urine should be thoroughly mixed with a 1 to 20 carbolic acid solution, or a solution of chlorid of lime, ½ pound to a gallon of water. The urinal, bed-pan, soiled linen, etc., should be boiled or soaked in one of the above solutions. The hands of the nurses and attendants must be scrubbed and disinfected with a 5 per cent carbolic acid solution or some equally good disinfectant.

Since every case of typhoid is the result of somebody's carelessness and as such carelessness is liable to persist it is desirable that people protect themselves by being immunized against the disease with typhoid vaccine. The tremendous value of this procedure was proved by the almost entire freedom of the United States military forces from typhoid during the World War in contrast to the high morbidity and mortality without such immunization in the Spanish-American War.

Children do not react from the immunization so severely as do adults; the procedure is practically painless and seldom interferes with school or play.

Typhoid vaccine composed of dead typhoid and paratyphoid "A" and "B" bacilli should be administered to children who live in communities where the disease is endemic, during an epidemic, and when they are traveling and are forced to partake of milk and water of unknown quality. All members of a household in which a case of typhoid occurs, as well as all individuals who come in contact with the patient, should be immunized.

Aseptic technic should be carefully observed, all syringes, needles, etc., being sterilized and the skin disinfected. The dosage in children is based on the body weight rather than the age. The weight of the average adult is considered as 150 pounds, so a child weighing 50 pounds should receive one-third the adult dose.

Medical.—There is no specific treatment for the disease itself. The general care and treatment of individual symptoms are the principal considerations in the treatment of typhoid fever.

Every case and every suspected case must be kept in bed. Even if the case is mild yet it is a source of danger to others. As the disease may last several weeks, the patient's strength must be conserved and protected by remaining in bed. A cheerful, well-lighted room with good ventilation should be chosen if the child is treated at home. The child should be trained to use a bed-pan so as to avoid any strain or unnecessary exertion. A case of typhoid requires skillful and continuous nursing and the services of both a day and night nurse should be secured, for the nursing and management of a case of typhoid are all-important. The nurse should be held responsible for the condition of the teeth, tongue and mouth. Bed-sores can be avoided by careful nursing, attention to the bed and bedding, frequent change of position, cleanliness and dryness. The child should be kept quiet and no visitors admitted to the sick room.

The diet is a great factor in treatment. Formerly it was taught that milk should be the exclusive article of diet. To-day there is a reversal of the teaching. Milk in many cases causes gas and distention, although some patients can digest it without discomfort. Kerley and many pediatricians forbid milk altogether in the diet of typhoid patients. The old method of starvation has been succeeded by a generous but non-irritating diet with high caloric value. Children have a much higher rate of metabolism than adults and require more food proportionately than adults. LaFetra some years ago treated typhoid patients in the pediatric wards of Bellevue Hospital on high caloric diets and the course of the disease was shorter, the children were more contented, and there was a gain in weight. If a child loses weight during this disease he is not receiving enough food. The child should be given all the food he desires and will digest. The following is a list of permissible foods:

> Soups—milk, potato, vegetable, etc., strained carefully
> Cereals—farina, oatmeal, etc., strained if containing rough particles
> Eggs—raw, soft-boiled, scrambled
> Meat—finely minced and scraped raw beef
> Milk toast without crusts

Ice cream, junket, blancmange, sherbet, soft part of baked or
stewed apples, orange and grapefruit juice
All liquids, including broths and cocoa

Water is as necessary as food. It should be given freely in the hope
of eliminating toxins through the urine. The rectum can be utilized to
introduce water into the system by means of the Murphy drip.

The fever can best be controlled by hydrotherapy. The tub baths and
the once popular Brand treatment should not be employed in young children.
The use of cold compresses and the cold wet pack gives as satisfactory results
without the shock and discomfort and handling in giving a tub bath. Cold
packs or an ice-bag to the head reduce the temperature and quiet the nervous
system.

The bowels require attention. A suitable dose of calomel in divided
doses can do no harm in the early stages and repeated at intervals of three
or four days. The lower bowel can be emptied daily with a low soapsuds
enema. Constipation does no harm if the rectum is emptied daily.

A certain number of cases develop diarrhea and this is the result quite
often of improper diet. If it becomes troublesome and excessive it should
be controlled with opium and bismuth. Two drops of tincture of opium
with 5 grains of subgallate of bismuth every two hours until relieved will
control this condition in young children.

Tympanites can be relieved by modification of the diet, eliminating milk
and reducing the fat or carbohydrate according to the individual idiosyn-
crasy. Turpentine stupes over the abdomen, pure glycerin and enemata,
etc., often give relief. The so-called intestinal antiseptics have very slight
effect. The administration of lactic acid bacilli or *Bacillus acidophilus* gives
decided relief in some cases.

The heart acts well in the majority of cases in children and it is not
necessary to give stimulants unless there are indications of a failing circula-
tion. If the pulse becomes rapid, 120 or over, the use of alcohol in large
doses is indicated. Alcohol gives better results than digitalis in typhoid
fever. Alcohol can be given in the form of whisky, brandy or sherry whey.
In collapse the hypodermic use of camphor oil is of benefit. Small doses of
strychnin have a stimulating effect on the heart.

Sleeplessness is a distressing symptom. The coal-tar products, such as
veronal, sulfonal, etc., are apt to depress the weakened heart. It may be
necessary to give small doses of morphin. Hyoscin, $\frac{1}{200}$ grain, gives
prompt relief in many cases.

Headache is an early symptom and appears before the heart muscle begins
to weaken. For this reason it is permissible to give small doses of aspirin
and phenacetin, combined with a small dose of caffein. A small dose should

be repeated every two hours until relieved. An ice-cap frequently gives much comfort.

The slight bronchitis in the early stage rarely requires treatment. If the cough is troublesome and prevents sleep, small doses of codein may control it. Paregoric in small doses at frequent intervals is effective.

The delirium may be controlled by reducing the fever, but a slight mumbling delirium requires no treatment. In violent cases hypodermics of morphin or hyoscin may be necessary.

Convalescence is apt to be slow and tedious and it will require all the resources of the nurse and family to keep the little patient contented and amused. Nervous fatigue is to be avoided by keeping the child from too much excitement from reading, playing, visitors, etc. After the temperature has been normal for a week the child may be allowed to sit up in bed on a bed-rest, then in a chair, and later in a chair in the sunshine by an open window. For several months after the illness care should be taken in the matter of exercising, for fear of straining the heart.

Release from Quarantine.—The typhoid patient ceases to be a menace to others only when typhoid bacilli are no longer to be found in his urine and feces, as evidenced by two or three consecutive negative tests on specimens taken at least twenty-four hours apart, but at an interval not greater than three days. The length of time that typhoid organisms persist in the excreta varies greatly, some patients ceasing to discharge the bacilli soon after convalescence is established, others failing to clear up for months and even years. When the latter happens the person is called a typhoid carrier.

The following information regarding such carriers and methods of relieving the condition is taken from a circular on the subject issued by the New York State Department of Health:

Sometimes a carrier discharges infectious material only at irregular intervals. In such case a large number of bacteriological examinations may be necessary before the condition is discovered.

Most typhoid carriers discharge the germs by way of the intestinal tract, but in a small proportion the infection is carried in the urine.

In the intestinal type of carriers the typhoid bacilli usually grow in the gall bladder or in the small ducts of the liver. When the seat of infection is in the gall bladder alone its removal may relieve the condition. Medical measures will usually cure the urinary type of carrier if treatment is begun during or soon after convalescence. The urinary carrier condition, however, may often be prevented if hexamethylenamine is administered during the course of the disease. In both the intestinal and the urinary type of carrier, if the condition is not cured by the methods stated, the carrier must expect to carry the germs of the disease throughout life.

Two specimens of excreta taken at least twenty-four hours apart, but at an interval not greater than three days, should be forwarded to a laboratory for examination. The specimens should be taken from a loose stool, either as the

result of a cathartic or otherwise and should be placed in the special glycerine outfits provided for this purpose. Every effort should be made to avoid delay in transmitting specimens to the laboratory.

PUBLIC HEALTH REGULATIONS

This disease is classified as a communicable disease and as such must be reported to the local health officer within twenty-four hours from the time the case is first seen. In New York State specimens of blood, urine and feces must be sent to the laboratory of the department or a laboratory approved by the State Commissioner of Health. It is also the duty of the attending physician to give detailed instructions to the nurse or other person in attendance in regard to the disinfection and disposal of the excreta. Such instruction is to be given on the first visit and shall conform to the special rules and regulations of the State Department of Health. When a case exists on any farm or dairy producing milk or its products for sale the physician in attendance shall report the case at once to the health department.

The summary of our present knowledge of typhoid as prepared by the Committee on Standard Regulations for the Control of Communicable Diseases of the American Public Health Association is as follows:

1. INFECTIOUS AGENT.—Typhoid bacillus, *Eberthella typhi*.

2. SOURCE OF INFECTION.—Bowel discharges and urine of infected individuals. Healthy carriers are common.

3. MODE OF TRANSMISSION.—Conveyance of the specific organism by direct or indirect contact with a source of infection. Among indirect means of transmission are contaminated water, milk, and shellfish. Contaminated flies have been common means of transmission in epidemics.

4. INCUBATION PERIOD.—From seven to twenty-three days, averaging ten to fourteen days.

5. PERIOD OF COMMUNICABILITY.—From the appearance of prodromal symptoms, throughout the illness and relapses during convalescence, and until repeated bacteriological examinations of the discharges show persistent absence of the infecting organism.

6. METHODS OF CONTROL
    (a) The infected individual and his environment
        1. *Recognition of the Disease.*—Clinical symptoms, confirmed by specific agglutination test and bacteriological examination of blood, bowel discharges, or urine.
        2. *Isolation.*—In fly-proof room, preferably under hospital conditions, of such cases as cannot command adequate sanitary environment and nursing care in their homes. Release from isolation should be determined by two successive negative cultures of stool and urine specimens collected not less than twenty-four hours apart.
        3. *Immunization.*—Of susceptibles in the family or household of

the patient who have been exposed, or may be exposed during the course of the disease.

4. *Quarantine.*—None.

5. *Concurrent Disinfection.*—Disinfection of all bowel and urinary discharges and articles soiled with them.

6. *Terminal Disinfection.*—Cleaning.

(b) General measures

1. Protection and purification of public water supplies.

2. Pasteurization of public milk supplies.

3. Supervision of other food supplies, and of food handlers.

4. Prevention of fly breeding.

5. Sanitary disposal of human excreta.

6. Extension of immunization by vaccination as far as practicable in communities where the disease is prevalent.

7. Supervision of typhoid carriers and their exclusion from the handling of foods.

8. Systematic examination of fecal specimens from those who have been in contact with recognized cases, to detect carriers.

9. Persons who fail to show a strongly positive Widal reaction and contemplate traveling, should protect themselves by vaccination.

10. Exclusion of suspected milk supplies pending discovery of the person or other causes of contamination of the milk.

11. Exclusion of water supply, if contaminated, until adequately treated with hypochlorite or other efficient disinfectant, or unless all water used for toilet, cooking, and drinking purposes is boiled before use.

CHAPTER XII

MALARIA

Definition.—A communicable disease transmitted not through persons but through the bite of a genus of mosquito known as Anopheles. Malaria is characterized by chills followed by fever of a remittent or intermittent variety accompanied with enlargement of spleen, anemia and general weakness. The symptoms are caused by the introduction of an animal parasite into the blood.

Synonyms.—Chills and fever, swamp fever, fever and ague, remittent fever; fièvre paludéenne, fièvre pernicieuse; Wechselfieber.

Historical.—Malaria is a disease that has been passed down through countless generations. Hippocrates gave an unmistakable description of malaria and referred to the dangers of swamps and stagnant waters and noted the enlarged spleen and the periodicity of the fever. Countess of Chinchon, the wife of the Viceroy of Peru, was cured of an intermittent fever by infusions of the bark of a Peruvian tree. A few years later her physician introduced the bark in Europe and it was given the name cinchona. Torti in 1753 coined the term "malaria" on account of the therapeutic effect of the "bark" on the type of fever in contradistinction to fevers uninfluenced by it. Several medieval writers suggested that the disease was due to minute parasites, and Lancisi in 1717 offered the theory that the parasites were introduced into the body by stinging insects. Virchow found pigmented particles in the red blood-cells of patients suffering from malaria. Laveran in 1880 discovered the plasmodium and its relation to malaria. He was a French army surgeon and much of his research and experimental work was done in Algiers. Ross, Grassi and others several years later were able to trace the life cycle of the parasite through the mosquito. Sambon and Low sent to Manson in England mosquitoes which had been infected. A typical attack of malaria was produced in his son who had been bitten by one of the mosquitoes. Bass and Johns in Panama in 1912 published an account of their success in cultivating the plasmodia from the blood of different types of malaria.

Etiology.—This disease occurs at all ages but young children are more frequently and more severely affected than adults. Cases of congenital malaria have been described in the literature where the disease is transmitted to the fetus through the placenta. It is also possible for the infant to be in-

fected during labor and the symptoms show a few days after birth. Deaderick believes that the percentage of children infected in a given locality can be taken as an index of the prevalence of malaria in that region. Cardamatis, as a result of a study of cases based on microscopic diagnosis, found that malaria is not as frequent in the first three months as in the following months of the first year, and that nursing babies possess a relative immunity.

The negro race is less susceptible as the mosquitoes do not bite negroes as eagerly as they do white persons. In malarial regions newcomers are more often affected than old residents although prolonged residence does not confer immunity. The season of the year has a decided influence as malaria does not occur when the weather is cold and the mosquitoes do not appear. They seem to require hot weather and it has been shown that the plasmodia do not develop within the mosquito at temperatures below 55° F. It is said that infected persons will recover spontaneously on going to a cold climate or to the mountains. The specific cause of malaria is an animal parasite of the class Sporozoa of the genus Plasmodium. There are three species:

1. *Plasmodium malariæ*, the parasite of quartan malaria which segments every seventy-two hours. This was the first discovered. It has six to twelve spores and its gametes are spherical when encysted. May sporulate equally in peripheral and visceral blood. Their ameboid motion is sluggish and the pigment is in larger quantities than in the tertian parasite.

2. *Plasmodium vivax*, the parasite of tertian malaria which segments every forty-eight hours. The young parasites are about one-fifth the size of a red blood-corpuscle and are actively ameboid. They are about the size of a red blood-cell when fully developed and are spherical and have from twelve to sixteen spores.

3. *Plasmodium falciparum*, the parasite of estivo-autumnal fever which segments either in twenty-four or forty-eight hours or may be irregular in segmentation. Its movements are active and its spores number from five to thirty. The gametes are most frequently crescentic in shape and appear only after the infection has persisted for at least a week. The infected red cells often become shriveled and have a dark and brassy hue. This is the parasite of the more severe and malignant type of malaria.

The Malarial Mosquito.—The most important mode of transmission is through the mosquito. It should be remembered that mosquitoes simply serve as hosts and do not have or cause malaria. They simply carry it from infected to healthy persons. Only one family of mosquitoes can carry the malaria parasite. This family is called Anophelines. Three spores are found in the United States and can be differentiated by their wing markings and the position they assume when resting. They prefer clear and pure water in which to deposit their ova. The common type of mosquito, the Culex,

prefers stagnant pools, tin cans, etc. The eggs are laid on the surface of the water and it takes usually forty-eight hours before the larval stage appears but it may be much longer in cold or unfavorable weather. The larvæ remain horizontal and this stage lasts from ten to thirty days and the pupal stage from two to five days. Minnows and small fish feed upon the larvæ.
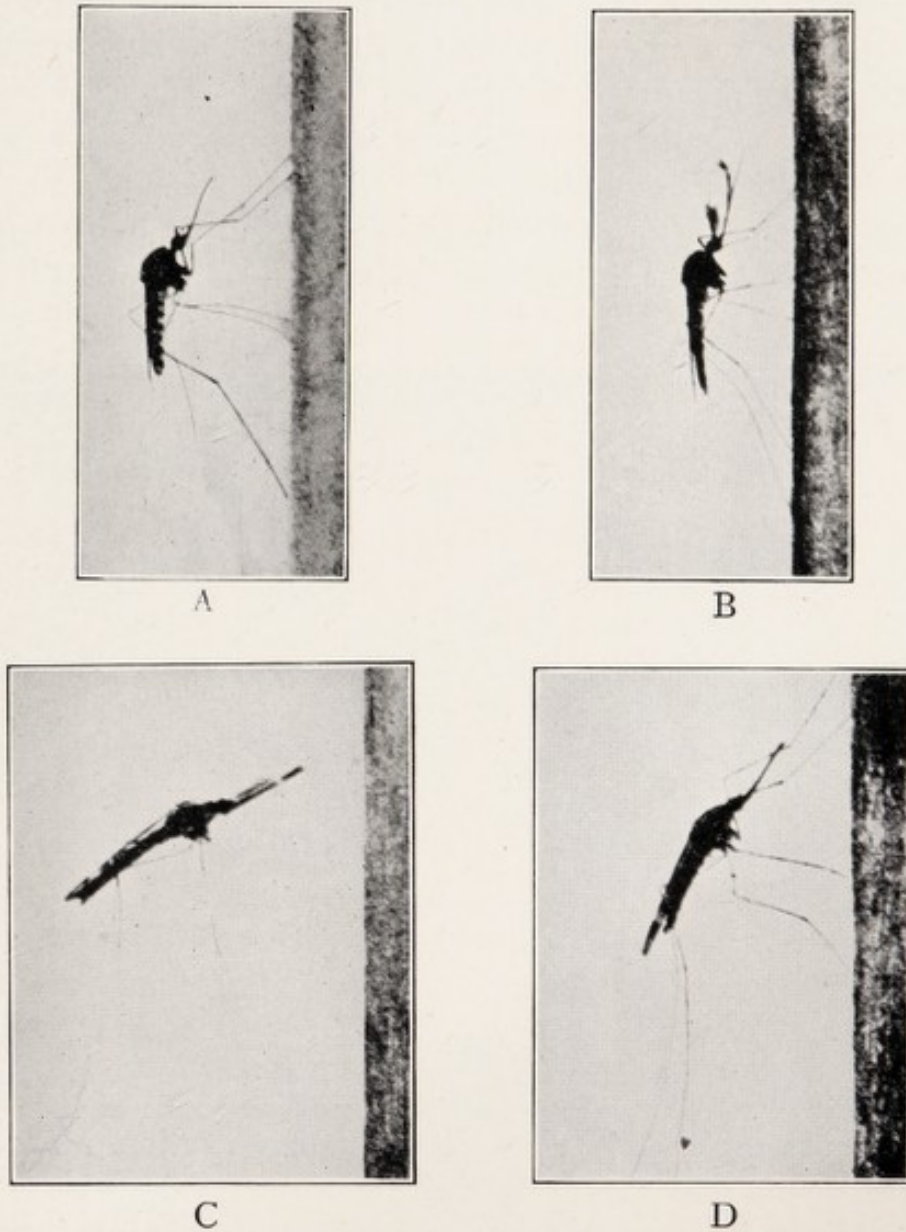
FIG. 12.—MALARIA.

A, non-malarial mosquito (male); *B*, non-malarial mosquito (female); *C*, malarial mosquito (male); *D*, malarial mosquito (female).

The malarial paroxysm is produced by a toxin which is liberated when the parasites sporulate. The tertian and quartan infections develop uniformly, one generation at a time, so the attacks show definite and typical periodicity. The estivo-autumnal parasites do not sporulate so uniformly, so the typical paroxysms do not develop and the fever may be very irregular or even continuous.

Pathology.—The action of the parasites is mainly on the red blood-cells and they produce a dark pigment which is deposited in the endothelium and in the adjacent cellular tissue.

The spleen is always involved and swollen. Its tissue is dark red or even black in color owing to the deposit of pigment. The parasites are more abundant than in any of the visceral organs. Microscopically one finds minute or diffuse necrosis and round cell infiltration. In chronic malaria the spleen is greatly enlarged with a thickened capsule. It is hard and flat and has a grayish or slatelike color. There is hyperplasia of the connective tissue with dilation of the veins.

The liver is not so frequently enlarged as the spleen. Fatty degeneration is uncommon and its color is dark and slatelike. The hepatic cells show evi-

FIG. 13.—MALARIA.
Mosquito (Culex) "wigglers," larvæ and pupæ, in the water

dences of cloudy swelling or they may become atrophied. The kidneys do not show so much pigmentation but they are increased in size. The convoluted tubules are dilated and show signs of degeneration. They may be blocked with débris stained with hematin.

The lungs may be pigmented, which should not be confused with anthracosis. The heart is often dilated and may show degenerative changes in the muscles. The endocardium may be pigmented.

Degenerative changes are found in the brain which is also pigmented.

The bone marrow is more deeply colored and is of firmer consistency than normal.

Fatal cases among children are not common, especially in the United States, so that opportunities to study the pathology as it concerns young children are infrequent. The lesions do not seem to differ materially from those observed in adults.
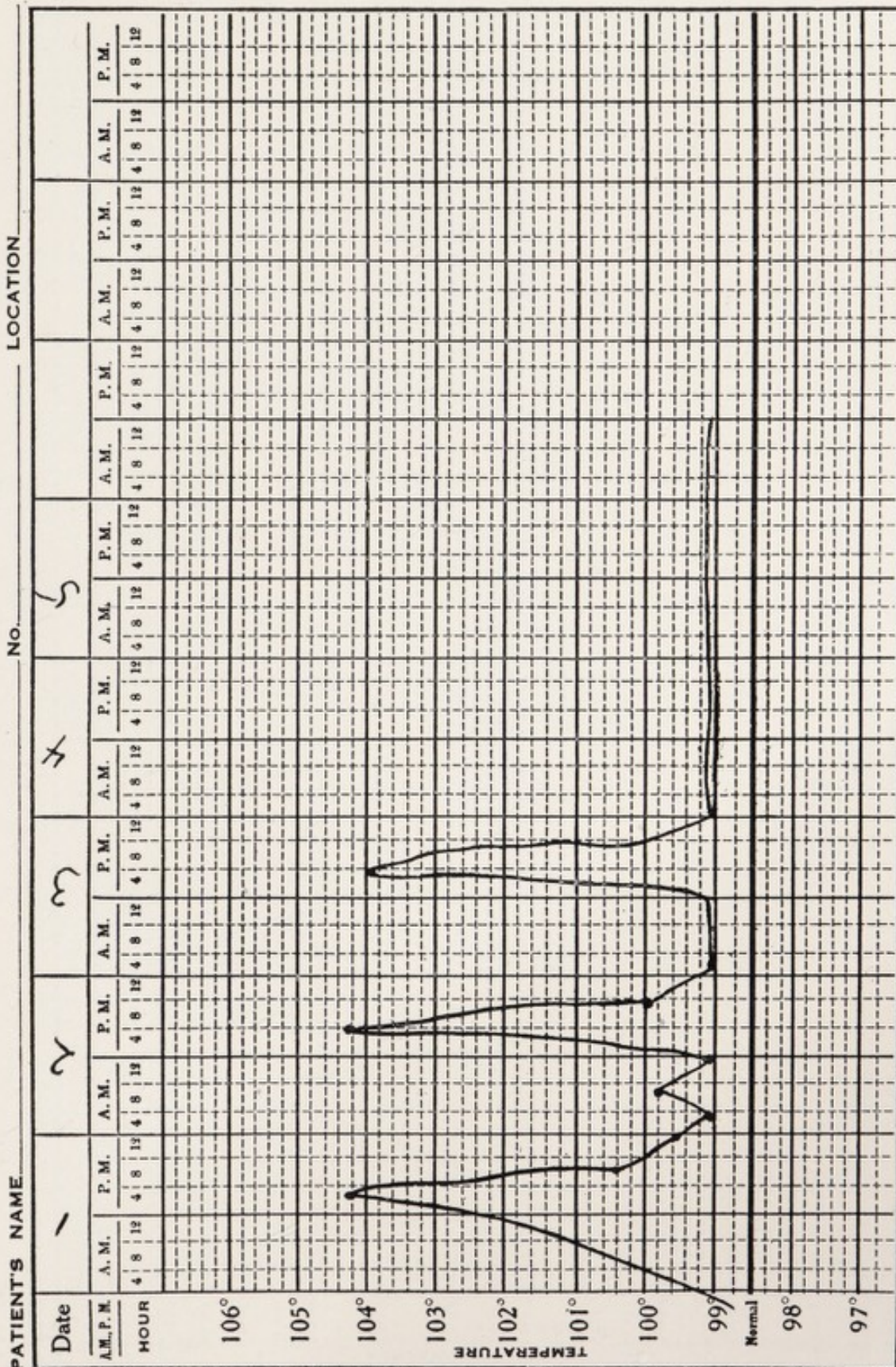
FIG. 14.—MALARIA. TERTIAN. CASE I.

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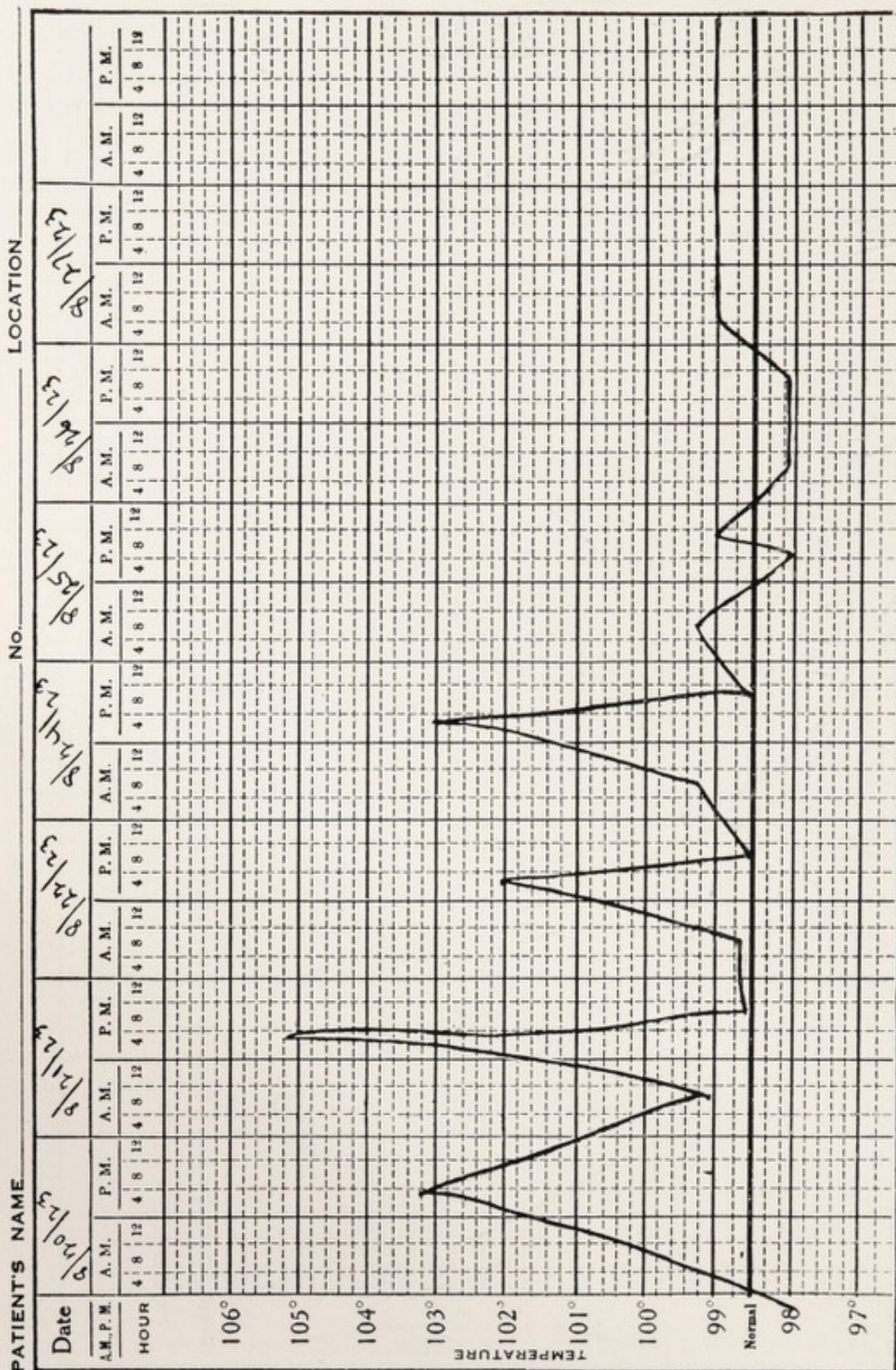
FIG. 15.—MALARIA. TERTIAN. CASE II.

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Fig. 16.—Malaria. Estivo-autumnal. Case III.

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FIG. 17.—MALARIA. ESTIVO-AUTUMNAL. CASE IV.

Symptoms.—The same clinical types of malaria appear in young children as in adults. In infants and very young children there is a marked variation in the stages of paroxysms. There is a short prodromal period in which the baby is restless and languid. The paroxysm does not always start with a chill. Mariottini reported 53 out of 120 cases of malaria in infants in which the chill was absent. When they occur they may be as violent as in adults. The nose, face and hands become cold. As the child grows older the chills become more severe. In young infants the chill may be replaced with a convulsion and vomiting occurs in most cases. The chills last from a few moments to about an hour and are followed by fever. The fever lasts from three to six hours and may even be continuous. It is relatively higher than in adults and may be as high as 106.5° F. Cardamatis, who examined the blood in 179 infants under two years of age suffering with malaria, found the tertian form in sixty-three, the estivo-autumnal in 106, the quartan in three and mixed infections in seven. Krauss and Mitchell collected statistics of 1,087 cases in children under sixteen years of age and of these 554 were estivo-autumnal, 203 tertian, four quartan, 216 continuous, forty-seven irregular and sixty-three unclassed.

The sweating stage is absent in infants; with the fall in temperature there is relief from all symptoms and the child will become active and lively and appear to be in excellent health. This continues until the next paroxysm appears. If unrecognized and untreated the paroxysms come on closer together and the case soon resembles one of continuous fever with wide variation in the peak of the temperature.

Gastro-intestinal symptoms are frequent in children. The most frequent are vomiting, diarrhea, anorexia, and coated tongue. When the disease has been present for some time the spleen is always enlarged. It is not so commonly enlarged in young infants. After the tenth year of life the spleen shows the same enlargements as in adults.

Symptoms on the part of the nervous system are frequent in children. Delirium and convulsions may accompany the febrile stage. Older children often complain of a severe frontal headache and neuralgia pains in the muscles. There may be choreic movements.

Pulmonary congestion is not uncommon in infants and gives rise to alarming and often obscure symptoms. The physical signs, râles, diminished respiration and bronchial irritation disappear with the fall in temperature, and may reappear with the next paroxysm.

Chronic Malaria.—This form of the disease is more common in children than the acute form. The most important symptoms are anemia, enlargement of the spleen and slight fever. This is called malarial cachexia. If untreated the child will develop severe malnutrition, muscular flabbiness and

extreme anemia. The fever may be so slight that it can only be recognized if the temperature is taken regularly several times a day.

Diagnosis.—The detection of the plasmodium and pigmented bodies in the blood makes a positive diagnosis of malaria possible. This is not difficult provided no quinin has been administered and the blood is obtained a few hours before the paroxysm.

The simplest method is to make an ordinary smear from a drop of blood on a clean slide. The film is fixed in absolute alcohol for one minute and then stained with an azure and eosin stain. This should be freshly mixed in the following proportions: water solution of eosin 1 : 500, 10 drops; water solution of azure II 1 : 500, 10 drops; distilled water, 30 drops. The slide is left in this solution for ten to fifteen minutes, then washed with distilled water and dried on filter-paper. This should first be examined under low power to find if the leukocytes are deeply stained and then use an immersion lens for studying the half-grown parasites and gametes. Several examinations may be necessary to find the parasites.

In conjunction with the blood examination the United States Public Health Service lays great importance on enlargement of the spleen. The examinations are made with the clothing loosened and the subject standing.

The therapeutic test is an important aid, for a fever which resists quinin which has been given in sufficient doses and for a sufficient length of time cannot be classed as malaria.

Typhoid fever can be diagnosed by the positive Widal test, lower pulse rate, and detection of bacilli in the stools.

Pyelitis in young infants, which is often accompanied with chills and irregular high fever, is recognized by the presence of pus cells in the urine, frequent urination and leukocytosis.

Septic conditions in addition to local and general manifestations have a marked leukocytosis.

Tuberculosis in children can be excluded in the diagnosis of malaria by the x-ray, physical examination and the examination of the sputum and blood.

Suspicions of malaria should be aroused by a history of exposure in a locality known to be malarial, by the periodicity of the symptoms, enlargement of the spleen, etc. Malaria is frequently overlooked in young infants when the cycle of symptoms is not definite and characteristic. The examination of the blood and the use of quinin should clear up any doubt in the diagnosis.

Prognosis.—Malaria in itself is not a fatal disease in children. The serious results come from a weakened constitution and a lack of resistance to intercurrent diseases and infections. Prompt diagnosis, administration

of quinin and removal when possible from the malarial locality will bring about a rapid and permanent cure.

Treatment.—*Prevention.*—There is probably no disease of such a serious nature that can be so completely controlled as malaria. The destruction of the mosquito and the parasites in the blood of human beings and protection from bites of mosquitoes are the means of prevention. The means for destruction of the mosquito are drainage of possible breeding places and the use of oil on the surface of the water to prevent the larvæ from obtaining air. All surface water should be drained and barrels, tin cans, gutters, etc., kept free from water. When this is not possible in swamps, stagnant water, etc., the use of crude oil is advisable. The oil forms a fine film over the water which makes it impervious to air and chokes the air tubes of the larvæ when they come to the surface to breathe. The oil can be sprayed from an ordinary water pot or by means of a force pump. Crude fuel oil is inexpensive and 1 ounce is sufficient to effectively cover 15 square feet of surface. The introduction of minnows and other small fish in ponds will help remove the larvæ as they feed upon them. The United States Public Health Service recommends dusting the breeding places with a dusting powder composed of one part of Paris green and 100 parts of sifted road dust. This is simple, cheap and very effective.

The adult mosquito can be destroyed in the home by closing a room and burning pyrethrum or sulphur powder.

All homes in malarial sections should be properly protected by screens. The mesh must be small enough to keep out small mosquitoes. The best size is 18 mesh screening which admits plenty of air. Both doors and windows must be screened and all cracks or crevices must be closed. Inside the house the beds and children's cribs should be carefully screened with mosquito netting. It must not be hung so loosely over the crib that the mosquitoes can find a way in or so placed that the body of the child can come in contact with it.

It is always advisable to isolate and screen every person suffering from malaria. This is so that the patient is not reinfected and also for the protection of the community.

Popular education of the public through lectures, pictures and literature as to the dangers of malaria and its relationship to mosquitoes and the simplest means of extermination and personal and household protection, is a most valuable agent in the prevention of this disease. Stringer estimates that malaria costs the United States over one hundred million dollars each year.

There are numberless examples of excellent results of well-organized campaigns against mosquitoes. Without such a campaign the Panama Canal could not have been built. The large army camps in the South were kept free from mosquitoes through efficient work by the Sanitation Corps. It is

the duty of public health authorities in malarial districts to see that mosquitoes are exterminated.

Destruction of the parasites in the blood stream of human beings is accomplished by the use of quinin. Quinin is also valuable in the prevention of malaria. Children when visiting in malarial sections should be given preventive doses of quinin. A good method is to give from 3 to 5 grains or two successive doses in each week.

Personal hygiene, such as regular hours, careful diet, suitable clothing, etc., is a valuable aid as it keeps the children in good health and less liable to infection.

Medicinal.—Quinin has proved to be a specific in the treatment of malaria, but unfortunately it is a difficult drug to administer to young children. There are a number of salts obtained from the cinchona bark which vary as to their solubility, palatability and efficiency. Laveran in 1881 demonstrated that a very weak solution of quinin killed the parasites and declared that the beneficial and specific action of quinin in malaria was the result of the destruction of the parasites.

The sulphate is used most frequently but it is very bitter and is apt to cause gastro-intestinal disturbance. The bisulphate is more soluble and rapidly absorbed and can be given to children in simple syrups, in chocolate syrup, or in yerba santa. The tannate of quinin has the advantage of being tasteless and is as effective as the other salts and well adapted for use in children. Euquinin is also tasteless and gives satisfactory results and is of value in treating malaria in children.

The best method of administration is by the mouth. The dosage depends on the age of the child and the severity of the attack. Children bear quinin in relatively larger doses than adults. Children often have difficulty in swallowing pills or capsules, so it is best given in solution. The so-called Roman method is to give a single large dose, 3 to 10 grains depending on the age of the child, from four to six hours before the expected paroxysm. The English method is to give the same single large dose in the sweating stage. Deaderick favors giving small doses at frequent intervals, for example:

> Under two years, 1 grain every three hours.
> Three to five years, 2 grains every three hours.
> Six to ten years, 3 grains every three hours.

He feels that when administered in this manner it is less liable to disturb the digestive and nervous systems. It is adapted to the various types or forms of the disease. The drug should be given during the night as well as the day. It should not be permanently discontinued as soon as the fever has stopped but only for twenty-four hours after and then given again for two

days with another interval of three days and gradually increasing the drug-less interval until it is given one day a week for at least a couple of months.

If it is impossible to give the drug by the mouth on account of vomiting it can be given hypodermically. For such use the bimuriate of quinin and urea is satisfactory in doses of from 2 to 5 grains. There are a number of disadvantages to the hypodermic use of quinin on account of the irritating effect on the skin which may lead to abscesses, sloughing, etc. For this reason it should be used only in infants who are very ill and in whom the diagnosis has been definitely established.

It is advisable to give a cathartic before beginning the quinin treatment. Castor oil, salts, or small doses of calomel may be given if there is time. The diet should be light and the child kept as comfortable as possible. During the stage of fever ice-packs and cool sponging can be used and hot applications and hot drinks will relieve the patient during the chill.

If there is any dyspnea or heart weakness, digitalis and adrenalin are of value.

There are a few individuals who have a real idiosyncrasy to quinin. Euquinin can be used in some of these cases successfully as it is free from the toxic properties of the other salts. Methylene-blue seems to have a specific action on the parasites. Salicylate acid and arsphenamin have been used with good effects.

In chronic cases and during convalescence the use of arsenic in addition to quinin is of undoubted value. Fowler's solution in one-drop doses gradually increasing to tolerance is the best method of employing arsenic.

Whenever practicable the child should be given a complete change of climate. Many cases recover in cold weather after a frost has appeared.

Public Health Regulations.—Malaria is included among the communicable diseases by the New York State Department of Health and as such must be reported at once to the local health officer.

As an example of the literature prepared for popular distribution the following issued by the New York State Department of Health is of interest:

Malaria is a dangerous communicable disease. Formerly it was responsible for a very large part of the deaths throughout the world. It is carried from person to person in only one way, namely, by the bite of a variety of mosquito (anopheles).

How to Prevent Malaria.—Do all you can to destroy mosquitoes. These insects breed in accumulations of water—or in the water among grass, weeds, etc., at the edge of ponds and streams. Do not allow such accumulations of water to exist on your premises. Look out for rain barrels, cisterns, open wells, tin cans, and sagging or clogged gutters on roofs. Empty them or keep them well screened.

Where water can not be removed from swampy areas by draining, the

breeding of mosquitoes can be prevented by sprinkling kerosene, or, better, a mixture of equal parts of kerosene, and crude petroleum in sufficient quantities to cause a thin film on the surface of the water. This must be done once a week to be effective.

Keep your house well screened. The malaria mosquito is smaller than the more common varieties, and a screen with a mesh of at least sixteen strands to the inch must be used to keep them out. Be sure that there are no holes in the screen or crevices around the edges through which mosquitoes can find their way. Avoid sitting out on an open porch in the early morning or evening. These are the times when the anopheles mosquitoes fly most frequently. Persons who enter the household in the evening are apt to carry a certain number of mosquitoes on their clothing. Care should be taken to brush them off just before entering. Sometimes it is found that mosquitoes gain an entrance in spite of all precautions. This is especially the case where there are children or other persons in the family who do not use sufficient care on coming into the house. When the anopheles mosquito has once succeeded in entering, it tends to remain in hiding during the day, particularly in the bedroom. Therefore it is a good plan to make a careful search for mosquitoes just before retiring. By killing all the mosquitoes in the room much may be accomplished, not only in preventing malaria but also in adding to personal comfort. One should remember that the anopheles mosquito is not so readily detected as the more common (culex) mosquito, because its "singing" when flying is not easily heard.

If you can not keep from being bitten by mosquitoes, you can keep from having malarial fever by taking quinine from May to November. An adult should take five grains every night before retiring. The method was used with great success in Panama in places where mosquito breeding could not be controlled. Children under ten years of age should be given one half as much as adults, but just as often. It ought not to be necessary to give quinine to babies as it is a simple matter to keep them from being bitten by mosquitoes through the use of mosquito netting.

Those who have had more than one attack of malaria, especially if the attacks have occurred in more than one year, need to be even more careful than other persons. They are not only just as liable to contract malaria again from infected mosquitoes but they may also have subsequent attacks resulting from parasites which may remain alive in their bodies, and, if bitten by anopheles mosquitoes, they may give the disease to others. For these reasons they should begin to take quinine as early as April and continue doing so until mosquitoes no longer fly. This should be done each year until they have been absolutely free from attacks of the disease for several years.

The easiest way to take quinine is in capsules. Sometimes it is easier to get children to take it in chocolates, in which the *tannate of quinine* should be used—in quantities twice as large as other forms of quinine.

Do not take "chill tonics," and other patent medicines of unknown composition. These are usually either more expensive than quinine, or less effective.

What to Do if You Have Malaria.—REMEMBER: The method given above is *not* the way to *cure* malaria if you have it. If you are taken with chills or fever, have a physician treat you. Quinine is used for treating malaria, but the dosage is different.

The National Malaria Committee recommends that cases of malaria should be treated continually for at least *eight weeks*. Sometimes longer treatment is

needed. Many persons give up their treatment when they feel well. This is dangerous. Unless the treatment is continued, the germs of the disease may still remain alive in the blood and cause later attacks even in the winter or the next year. Even if the disease does not become active, mosquitoes may carry it to other members of the family or to your neighbors, unless the treatment is kept up.

The report of the Committee of the American Public Health Association on the Control of Communicable Diseases contains the following synopsis of malaria:

1. INFECTIOUS AGENT.—The several species of malarial organisms— *Plasmodium vivax* (tertian); *Plasmodium malariæ* (quartan); *Laverania falciparum* (æstivo-autumnal.)

2. SOURCE OF INFECTION.—The blood of an infected individual.

3. MODE OF TRANSMISSION.—By bite of the infected Anopheles mosquitoes. The mosquito is infected by biting an individual suffering from acute or chronic malaria. The parasite develops in the body of the mosquito for from ten to fourteen days, after which time the sporozoites appear in its salivary glands.

4. INCUBATION PERIOD.—Varies with the type of species of infecting organism and the amount of infection; usually fourteen days in the tertian variety.

5. PERIOD OF COMMUNICABILITY.—As long as the malaria organism exists in the blood.

6. METHOD OF CONTROL

    (*a*) The infected individual and his environment

        1. *Recognition of the Disease.*—Clinical symptoms, always to be confirmed by microscopical examination of the blood. Repeated examinations may be necessary.

        2. *Isolation.*—None except protection of the patient from approach of mosquitoes by screening his bed or room or house, until his blood is rendered free from malarial parasites by thorough treatment with quinine.

        3. *Immunization.*—None. The administration of prophylactic doses of quinine should be insisted upon for those constantly exposed to infection and unable to protect themselves against Anopheles mosquitoes.

        4. *Quarantine.*—None.

        5. *Concurrent Disinfection.*—None. Destruction of Anopheles mosquitoes in the sick room.

        6. *Terminal Disinfection.*—None. Destruction of Anopheles mosquitoes in the sick room.

    (*b*) General measures

        1. Employment of known measures for destroying larvæ of anophelines and the eradication of breeding places of such mosquitoes.

        2. Blood examination of persons living in infected centers to determine the incidence of infection.

        3. Screening sleeping and living quarters; use of mosquito nets.

        4. Killing mosquitoes in living quarters.

CHAPTER XIII

POLIOMYELITIS

Definition.—Poliomyelitis is an acute systematic disease which in a certain proportion of cases involves the central nervous system. In these cases it generally attacks the gray matter of the anterior horn but may involve other portions of the brain and cord. This results in paralysis in a certain percentage of cases which may be more or less permanent and may be either flaccid or spastic according to the motor neurons involved.

Many cases have only slight general symptoms and may escape diagnosis. These are called abortive or non-paralytic cases.

The disease may appear in epidemics but more frequently occurs sporadically.

Synonyms.—The United States Census Bureau in a report in 1919 collected twenty-four different names for this disease and suggested that a single term be adopted.

They proposed the term poliomyelitis, derived from the Greek words *polios,* meaning "gray," and *myeloa,* meaning "marrow."

Among the terms under which the disease has been described may be mentioned infantile spinal meningitis, acute spinal paralysis, anterior poliomyelitis, poliomyelitis anterior acuta, dental paralysis, Heine-Medin disease, infantile paralysis, epidemic infantile paralysis, etc.

HISTORY

Ancient medical books contain no reference to or description of this disease and it seems to be of comparatively recent origin. A disease so striking in its symptoms and chiefly affecting young children could hardly have been overlooked by the medical writers of olden times, especially if it occurred in extensive epidemics. Probably the first accurate description of this disease was made by Underwood, in whose treatise on *Diseases of Children,* published in 1784, are two pages in which he calls attention to a condition he describes as "debility of the lower extremities." This account is of historic interest and the following quotation is taken from Ruhräh:

Debility of the Lower Extremities.—This disorder is not noticed by any medical writer within the compass of my reading, or is not so described as to ascertain the disease here intended. . . . If it arises from teeth, or foul bowels, the usual remedies should be employed; and have always effected a cure. . . .

The first thing observed is a debility of the lower extremities, which gradually become more infirm, and after a few weeks are unable to support the body.

When only one of the lower extremities has been affected the above means in two instances out of five or six entirely removed the complaint; but when both have been paralytic, nothing has seemed to do any good but irons to the legs, for the support of the limbs, and enabling the patient to walk. At the end of four or five years, some have by this means got better in proportion as they have acquired general strength: but even some of these have been disposed to fall afterward into pulmonary consumption, where the debility has not been entirely removed.

A very accurate description of the acute onset of the disease was made by Jörg in 1816. His account went on to state: "The little girl was born healthy, when a few weeks old she suffered from some violent fever . . . which seemed to have been caused by a chill and to be of the nature of those typhoid fevers to which children are so subject. . . . The illness lasted a long time . . . the child gradually recovered from the fever although she remained for a long time wasted and weak . . . the mother noticed she did not move the feet properly and it became more and more clear that the feet were becoming clubbed."

The literature on this subject subsequently became more frequent but the first complete monograph did not appear until 1840. It was written by Heine, a German orthopedist and was entitled *Observations concerning Paralysis of the Under Extremities and Their Treatment*. It was a volume of seventy-eight pages with seven full-page plates. The second and enlarged edition was published in 1860 and contained 204 pages with fourteen plates. In this the title was changed to *Infantile Spinal Paralysis*. This name was selected because he believed it affected children only. All the adults he had seen who had had the disease had been stricken with it in childhood. West describes the disease in his well-known textbook on *Diseases of Children* published in London in 1848.

The first epidemic reported in this country broke out in Louisiana in 1841 and was described by George Colmer. He found ten cases of either hemiplegia or paraplegia had occurred within a few months in a small locality. He stated that "the cause seemed to be the same in all, namely, teething."

Sir Walter Scott was a victim of the disease. In his autobiography he wrote: "I shewed every sign of health and strength until I was about eighteen months old. One night, as I have often been told, I shewed great reluctance to be caught and put to bed. In the morning I was discovered to be affected with the fever which often accompanies the cutting of large teeth. It held me three days. On the fourth when they came to bathe me as usual they discovered that I had lost the power of my right leg." He goes on to describe how a number of physicians, including his grandfather, John

Rutherford, who was professor of medicine in the University of Edinburgh, could find no dislocation, strain or any cause for paralysis. His grandfather had him sent to the country to live in order that he might have plenty of fresh air. A persistent course in inducing him to take gentle exercise was followed for several years. He made an excellent recovery, and, although his lameness never left him, he was able to enjoy long walks and was an expert horseman. Some of the early terms used to describe this disease, such as "dental paralysis," "teething paralysis," "paralysis during dentition," showed the tendency to attribute this ailment of young children to the natural process of teething. While all of the earlier writers attributed this disease to weaning or teething, credit is due to Heine for recognizing that he had to deal with a disease of the spinal cord.

After Heine's second edition was published in 1860, very little of scientific or historical importance appeared until Strumpell gave the first accurate account of the cerebral type of the disease in 1884. He called attention to the fact that there was a close resemblance between certain cases of encephalitis with spastic paralysis in children and cases of infantile spinal paralysis. He suggested for the first time that an external infective agent was responsible for both conditions.

At the International Medical Congress in 1890, Medin, a Swedish physician, gave an elaborate clinical account of cases he had studied during several epidemics in Sweden. On account of his clear clinical picture the Germans, with their fondness for linking physicians' names with diseases, called it the Heine-Medin disease. Medin merely claimed the disease to be contagious. While epidemics had been recognized before yet the infectious character had not been suspected.

A student of Medin named Wickman studied and described an epidemic in Norway in 1905 and wrote perhaps the most valuable monograph on poliomyelitis that has yet appeared. His classification is generally accepted and he first described the so-called abortive or non-paralytic cases.

Flexner and Lewis in 1909 were among the first to fully transmit the disease from one monkey to another. They were able to prevent the development of the disease in monkeys by the administration of blood-serum from monkeys or from human beings who had recovered from the disease. Flexner with Noguchi in 1913 demonstrated the responsible organism. They showed that it was a living virus capable of passing through a porcelain filter which would keep back ordinary bacteria, and that it was not merely a toxin.

EPIDEMIOLOGY

Before Wickman's monograph appeared, the fact that the disease could exist in a non-paralytic form was not known and thus the only epidemics

reported were those in which the cases were definitely paralyzed. Medin and Wickman emphasized its contagious character and pointed out the probability of carriers in the dissemination of the disease.

The knowledge that paralysis occurred in only a small percentage of the cases changed the attitude of the medical profession in regard to the disease and its mode of transmission. On account of its epidemic character it must be a communicable disease.

Its virulence seems to vary in different epidemics and in different localities. In some it seems to have a greater tendency to involve the nervous system than in others.

Geographical Distribution.—The first epidemic reported in this country was in 1841. A small epidemic was noted in Norway in 1868 and in Sweden in 1881. Since then they appear to have been more frequent and more widely distributed. The disease has been reported and exists endemically or sporadically in practically all the countries in Europe, North and South America, the West Indies, Australia and the South Sea Islands. The 1905 epidemic in Norway and Sweden was severe, widespread and devastating. A similar epidemic occurred in the United States in 1916. Ruhräh gives a list of 149 epidemics that have been reported from 1841 to 1911. The United States epidemics from 1916 to 1924 have received much attention from the public press and have aroused a popular fear or frenzy regarding the disease. The popular belief is that every child who contracts the disease will either die or become a cripple for the rest of his days.

The disease, while it has appeared in epidemics in the large cities, is more frequent in the country and sparsely populated districts. It seems to be a rural disease and something in rural life and surroundings seems to favor its development and dissemination.

The death rate for poliomyelitis is much greater in the rural than the urban districts, as is shown by the statistics of the New York State Department of Health. The rate per 100,000 population was:

Year	Urban	Rural
1924	1.4	2.4
1925	1.8	2.6

Frequency.—This is difficult to state on account of the large number of abortive or non-paralytic cases. It has been estimated that about 80 per cent of the cases do not result in paralysis. Most statistics include only cases of paralysis. In New York State there were over thirteen thousand cases reported in 1916, the year of the great epidemic, but it is probable there were in reality over thirty thousand cases.

As the true character of the disease is now generally recognized by the

medical profession, the number of reported cases seems greater the past twenty years than in any previous period. There are no doubt a great many cases in which the diagnosis is not made, even though there may be some resulting paralysis. It is not at all infrequent that the true character of the trouble is not even suspected until a long time after the acute stage of the disease and then only because of a slight weakness or deformity of the feet or a single muscle.

It is a well-known fact that there is a great variability in the infectivity of the various infectious diseases. Frost of the United States Public Health Service considers poliomyelitis to be only about one-fifteenth as infectious as scarlet fever.

Season.—It was formerly believed that poliomyelitis was distinctly a summer disease but a number of winter epidemics have been reported both in this country and in Europe. There is no doubt it shows a decided predilection for the warm, dry summer months. The great majority of cases and of epidemics occur between the months of May and November.

The number of cases show a marked decline after the cold weather sets in. In the southern hemisphere the greatest number of cases occurs from December to May, which corresponds to the summer and autumn of our northern latitude. It is of interest to note that epidemics of other infectious diseases of children, such as measles, scarlet fever, etc., are more frequent during the winter months and are uncommon during the summer months.

Transmission.—The exact method of transmission is not yet definitely known, but from our present knowledge it appears that human beings and their activities are responsible for the dissemination of this disease. The rôle of domestic animals or insects in spreading the disease has not yet been settled.[1]

Among the vast literature bearing on the transmission of poliomyelitis are a number of instances where paralytic disease in domestic animals occurred during epidemics. For example, a farmer had a herd of eighteen calves in Vermont on a farm where a young adult had been stricken with the disease. Five of these became ill and paralyzed within ten days. The paralysis affecting the dogs after distemper, and also chickens, has been thoroughly studied and as yet no one has been able to demonstrate any direct relation to poliomyelitis in man, for the pathologic changes in these cases are distinctly different. Insects, such as the flea, mosquito, bedbug, louse and fly, have been carefully studied to see if they were capable of transmitting the disease, but no evidence of their guilt or possible guilt has been found.

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[1] While the paralytic conditions which are seen not infrequently have no connection with or similarity to poliomyelitis, yet it has been found that monkeys, rabbits and probably guinea-pigs are susceptible to this disease.

Richardson claimed that rats were capable of transmitting the disease, but his evidence was purely circumstantial and no proof has been forthcoming from laboratory and experimental studies.

Saunders, on the other hand, is a firm believer that the green bottle fly, *Lucilia Cæsar*, is the carrier of the virus. He claims to have experimental proof of this contention. This fly deposits its eggs on decaying animal and vegetable matter and often selects food or an orifice of the human body; also in the ears, the nose, the anus, and more frequently upon the milk ducts of mammalians. Hence the frequent occurrence of paralysis in sucking animals.

It is possible for insects to become contaminated with the virus and deposit it on food. Experiments have shown that flies contaminated with the virus may retain it in active state as long as forty-eight hours after exposure. Such insects, therefore, may possibly become passive carriers of the disease. While this may happen under experimental conditions yet it has not been shown that they do so ordinarily.

Route of Travel.—The fact that epidemics of poliomyelitis in common with other communicable diseases spread along the line of human travel has been noted by many writers. A study of the spread of epidemics shows that while there is a tendency to a grouping of cases, yet the outbreaks follow closely the arteries of human intercourse. This is an argument in favor of the transmission of the virus by human agents and is an important point in the epidemiology of this disease.

Nevertheless poliomyelitis breaks out in isolated and inaccessible regions and makes long jumps over counties and towns. In a Massachusetts epidemic 70 per cent of the cases were found one-quarter of a mile from a railroad. In the New York epidemic of 1916 there was a decided tendency for the disease to spread along the waterways.

Food.—Careful and extensive research work has been done to determine whether this disease may be transmitted by any particular type of food. Only one instance of a milk-borne outbreak of poliomyelitis has been found in the literature, namely, a series of eight cases in Cortland, New York, during December, 1925, recorded by Knapp, Godfrey and Aycock in the *Journal of the American Medical Association*, August 28, 1926. Breast-fed babies who never had a drop of cows' milk are known to have contracted poliomyelitis and the disease has also occurred in children who had been fed only on pasteurized milk. It is possible that uncooked food may become contaminated with the virus and so carry the disease, but this is very improbable.

Sewage.—This disease does not bear any similarity to any of the intestinal diseases transmitted through the discharges of the bowels. It is very

doubtful if the virus is active after passing through the intestinal tract. It seems to bear no relation whatever to the method of sewage disposal.

Dust.—Several investigators have found the virus in dust swept from the floor of a patient's room. This is not common and as the virus will not remain active under such conditions for more than forty-eight hours, dust becomes a negligible factor in the transmission of the disease.

Human Carriers.—The present view in regard to the transmission of poliomyelitis is that a human carrier, active or passive, is the main source of infection and that its spread and extension results from contact with patients ill with the disease or with healthy carriers. Flexner sums up the situation as follows: "The microbic agent of epidemic poliomyelitis is present in the nasal and buccal secretions and is carried by persons, not insects, and communicated by them in such manner as to gain access to the upper respiratory mucous membranes of other persons among whom a portion, being susceptible to the injurious action of the virus, acquire the infection and develop the disease."

During 1917, the Research Laboratory of the Vermont State Board of Health studied the prevalence of carriers in Vermont. The report of examinations of the family of four children published in the *Journal of Experimental Medicine* furnishes an instructive illustration of the mode of infection of the disease as brought out by clinical and experimental study. It establishes more firmly the carriage method and describes for the first time the occurrence of two carriers in the same family and transmission of the virus during the incubation period of the disease. All of the four children showed symptoms of poliomyelitis in varying degree. The source of infection and periods of incubation have been followed. By inoculation two of the children were shown to carry the virus of poliomyelitis in the nasopharynx. Of these, one was detected to be a carrier after recovering from a non-paralytic attack of the disease, and the other was discovered to be a carrier about five days before the initial symptoms, attended later by paralysis, appeared. The original case from which the three others took origin was fatal; the youngest child, after quite a severe onset, was treated with immune serum, and made a prompt and almost perfect recovery. The nasopharyngeal secretions of two of the cases, taken one month after the attack, proved incapable of neutralizing an active poliomyelitis virus.

The proposition is presented that every case of poliomyelitis develops from a carrier of the microbic cause, or virus, of poliomyelitis.

ETIOLOGY

Age.—This is essentially a disease of early childhood, for the great majority of cases occurs between the first and tenth years of life. The

popular term "infantile paralysis" is neither accurate nor descriptive, since in the larger proportion of cases no paralysis appears. Moreover it is liable to occur in adults as well as in young children and only seldom in young infants. It has been estimated that about 90 per cent of all cases are found in children under ten years of age. There may be variations in different epidemics. For example, 25 per cent of all cases in the Norway epidemic of 1911, were in adults as compared with 12 per cent in Iowa in 1910.

Cases in very young infants are very rare, the youngest case being reported by Duchenne in a baby twelve days old.

Sex.—It has been shown in an analysis of reported cases from many sources that a greater proportion of males are affected than females. The ratio may be as high as 60 to 40. This is more apt to be the case in adults, while in very young children the difference is less. The disease also seems to be more severe in males than in females.

Race.—There seem to be no race restrictions to this disease. The white man, the black man and the yellow man are all victims of poliomyelitis.

Social and Hygienic Conditions.—This disease is no respecter of the social status of the individual. It affects alike both the rich and the poor, the clean and the unclean. Unhygienic living conditions, such as overcrowding and uncleanliness, are not predisposing causes. This is not the case in many diseases.

Teething.—Many of the earlier writers claimed teething to be the predisposing factor, but this has not been proved to have any influence. The fact that the teeth begin to erupt at the age when the child is most susceptible to the disease proves nothing. It is so easy to blame every ill and every indisposition that may affect the very young child to this cause. Over half of the cases are in patients who are over five years of age in whom the question of dentition cannot be a factor. As the point of entry of the virus is through the nasal or faucial mucous membrane, the condition of the tonsils and adenoids is of greater importance than the teeth. It is quite possible that carious teeth may harbor the virus. A few studies have been made in regard to tonsils and poliomyelitis and it has been shown that children who have had their tonsils removed are less susceptible to the disease than those who have not.

BACTERIOLOGY

Prior to 1909 when Landsteiner and Popper produced typical poliomyelitis in a monkey by injecting an emulsion of the spinal cord from a fatal case, no definite results in producing experimental poliomyelitis had been reported. The earlier investigators looked for microörganisms in the spinal fluid. A number of observers isolated diplococci which they claimed

were the causative agent. Giersvold, in 1905, studying cases in the Norwegian epidemic of that year, found Gram-positive cocci in the cerebrospinal fluid of twelve cases. He claimed to have inoculated animals with these germs and produced paralysis and death. None of these diplococci or cocci were able to meet Koch's postulates, and scientific workers were not convinced of their relation to poliomyelitis.

In 1913 Flexner and Noguchi published an account of their experimental work in detecting and isolating the microörganism causing poliomyelitis. This organism, which was grown under special conditions from brain and cord tissue of typically affected monkeys, appeared as a globoid or small coccus in pairs or short chains. It is capable of passing through the pores of a Berkefeld filter. It is extremely small and usually occurs in pairs, short chains or small groups. It is strictly anaërobic and grows best on human ascitic fluid. These anthras have been found in the brain and spinal cord of fatal cases and when inoculated into monkeys have set up a typical poliomyelitis.

Another group of observers headed by Rosenow and his coworkers claim to have found a streptococcus in the brains and cords of fatal cases. This organism is said to be polymorphous and in one stage may resemble globoid bodies and pass through a filter.

Kolmer, Brown and Freese found four different kinds of microörganisms in fatal cases of poliomyelitis. They were streptococci, diplococci, diptheroid and Gram-negative bacilli. It would seem that these organisms are terminal infections or play a secondary rôle in poliomyelitis.

There exists at the present time no unanimity of opinion among scientists as to the definite and positive causative factor, but the majority feel the causative agent is not a bacterium but is probably a globoid filtrable body.

Virus.—The virus is very resistant. Neither freezing nor a 50 per cent glycerin kills it. It is less resistant to heat and is destroyed at a temperature of 45° C. in one half hour. Antiseptic solutions readily prevent its growth. Drying does not kill the virus which is of practical importance in the handling and the dissemination of cases. It is capable of living in the nasopharyngeal mucous membranes for many months. Healthy carriers. are perhaps not uncommon and Lucas has reported a case in which the virus remained active for two years and three months.

Our present knowledge of the virus and its presence in and exit from the human body has been well summarized by Frost of the United States Public Health Service.

Sources of the Virus.—In the human body the virus has been found:

(a) In the tissues and secretions of persons dead of poliomyelitis, namely, in the brain, the spinal cord, the mesenteric glands, the tonsils, and in the mucous secretions of the nasopharynx, the trachea, and the intestines.

(b) In the secretions of persons acutely ill with poliomyelitis, namely, in the nasopharyngeal secretions and in washings from the rectum. The infectivity of these secretions has been demonstrated not only in persons suffering from the clinically typical paralytic forms of poliomyelitis, but also, though less conclusively, in the secretions of those suffering from mild, clinically indefinite, abortive forms.

(c) In the nasopharyngeal and intestinal secretions of persons convalescent from acute attacks of poliomyelitis. Although the total number of recorded examinations of convalescents is as yet small, the results of studies by Kling, Wernstedt, and Petterssen suggest that in a very large proportion of persons recovering from poliomyelitis these secretions remain infective for several weeks or even months.

(d) In the nasopharyngeal secretions of apparently well persons who have been more or less intimately associated with cases of poliomyelitis, chiefly in epidemic foci. No figures are available as yet to form an estimate of the proportion of persons who, upon exposure to infection with poliomyelitis, become "carriers," or of the relative proportions of carriers and clinically recognizable cases of poliomyelitis in an epidemic focus. The technical difficulties in the way of demonstrating the virus, which involves the injection of filtrates into monkeys, are such that extensive statistics upon this point can hardly be expected in the near future, unless the technic of the demonstration can be greatly simplified.

Outside of the human body the living virus has been demonstrated in nature only in the dust of rooms occupied by poliomyelitis patients and presumably contaminated with their secretions, and possibly (though the demonstration is not fully convincing) upon articles recently handled by persons suffering from poliomyelitis.

In brief, there is at present experimental proof of the following sources of infection: The secretions of persons ill with poliomyelitis, those convalescent from the infection, and "passive carriers," that is, persons apparently well who are harboring the specific virus and discharging it in their secretions.

Avenues and Vehicles of Infection.—As to the avenues through which the virus may enter the human body to cause infection, inference may be drawn chiefly from experiments upon lower animals. Monkeys may be experimentally infected by injection of the virus directly into the brain, or the subdural space, into the general circulation, the peritoneal cavity, or even into the subcutaneous tissue. They may also be infected by rubbing the virus upon the scarified mucous membrane of the nose, and even by rubbing it upon the uninjured mucous membrane. Also, by the use of massive doses of the virus and under quite artificial conditions, it has been

found possible to produce infection by feeding monkeys through a stomach-tube.

Of the various methods of infection experimentally shown to be possible, infection through the nasal mucosa appears to be the most constant under conditions which might be approximated in nature.

Concerning the natural vehicles of infection, experiments performed under laboratory conditions are necessarily somewhat inconclusive. The infectiousness of the nasopharyngeal and intestinal secretions of infected persons and the susceptibility of monkeys to infection through the nasal mucosa indicate very strongly that the disease may be transmitted in nature by such vehicles as may serve to transmit these secretions from infected persons to the respiratory (or digestive) tracts of others, that is, by more or less direct personal contact. The resistance of the virus to the influence of drying and sunlight suggests the probability of the infective agent being conveyed in dust and in fomites, a suggestion strengthened by the experimental evidence of the infectivity of dust from the sick room.

Experiments showing the possibility of transmitting the infection from monkey to monkey through the agency of a biting fly, *Stomoxys calcitrans*, and in one instance through the bedbug, have added considerable weight to the hypothesis that poliomyelitis is in nature an insect-borne disease. However, since the transmission of the disease through these insects has proved possible only in isolated instances and under highly artificial conditions, these experiments do not warrant the conclusion that stomoxys or other insects play any important part in the natural dissemination of the disease in man.

On the whole, the experimental evidence, taken alone, while not excluding other means of transmission, points to the conclusion that poliomyelitis is a contagious disease, spread from person to person through interchange of infectious secretions, the sources of infection being the clinically definite and clinically indefinite acute cases of poliomyelitis, convalescents, and passive human carriers.

PATHOLOGY

The older pathologists considered poliomyelitis a local disease with the lesions centered in the anterior horns of the cord. To-day we know that it is a general infection which affects not only the nervous system but various organs and lymphoid structures. These changes may be so slight in some of the cases that they produce very mild symptoms, which accounts for the abortive or non-paralytic cases and those with only a transient paralysis. In others, lesions are only of moderate severity and the paralysis which seems extensive at first tends to clear up. Ultimately the resulting paralysis is trifling compared to that which is seen at first. Then there are very serious

cases in which the damage is permanent, the existing paralysis does not clear up and the destruction may reach the respiratory and other brain centers and cause death.

Temporary or transient paralysis results from edema causing pressure on the cells. Permanent paralysis results from actual destruction of the ganglion-cells and its extent varies with the number involved and their location. The lesions may be located in any part of the nervous system and are often more extensive and severe than the symptoms would indicate.

The gross appearance of the brain and cord in fatal cases is characteristic. The inflammation process often involves the entire length of the cord. The dura is congested and the pia injected and edematous. The organs are of grayish-pink color. On section of the cord the gray matter shows the same pinkish color and bulges slightly. There may be small hemorrhagic points through the tissue of the cord.

The changes in the central nervous system are most marked about the blood-vessels. In the early stages there is an infiltration of small round cells through the pia and a large number of cells about the vessels within the thin perivascular lymphatic sheaths. The walls of the vessels are infiltrated and their lumen narrowed. The changes are most marked when the cord is most vascular, namely, in the cervical and lumbar regions, and particularly in the anterior portion and its anterior fissure in which the vessels run which supply the anterior part of the cord. Less frequently changes take place in the posterior horns and rarely in the white matter. Draper has indicated that these types of histological disturbance may be made out; first a perivascular infiltration where there is a broad column of tightly packed lymphocytes pressing like a close-fitting collar around the lumen. Second, an interstitial lesion consisting of a few polynuclears, scattered mononuclears and frequent extravasations of red cells which may be so extensive as to be called "hemorrhagic extravasation." Third, parenchymatous changes which consist of necrotic deteriorations of the ganglion-cells of the anterior horns. As this advances polynuclear leukocytes appear which dispose of the débris, thus forming the characteristic neurophages. It is not possible to state how much of this damage is due to toxic action and how much is due to mechanical causes such as pressure.

Similar changes may be noted in the pons, medulla and cerebrum. The lesions follow the distribution of the blood supply. The changes are especially related to the pia and blood-vessels and there are areas of infiltration with mononuclear cells and deterioration of the ganglion-cells.

The changes in the old cases consist of atrophy of the cord which is most often limited to one lateral half. There is great variation owing to differences in the amount of destruction in the original disease. The general changes are of a sclerotic character. The ganglion-cells in the af-

fected anterior horn are either entirely wanting or diminished in number or so shrunken that they can scarcely be recognized. The fibers of the anterior horn are atrophied as are the nerve trunks and degenerative changes have taken place. The white matter is affected but to a less extent.

There is degeneration and atrophy of the nerves and muscles themselves. The affected muscles are atrophied and are often degenerated. There may even be a complete absence of muscle-fibers which are replaced by fibrous and fatty tissue. The affected extremities grow more slowly and the bones are smaller and show atrophy. As the child grows there are often shortening of these extremities and deformities as a result of the effect of the paralyzed muscles.

Lesions are found in the lymphatic and parenchymatous organs of the body consisting in enlargement of the nodes, especially in the intestines and mesentery.

Small round-cell infiltration is seen in the portal spaces of the liver.

There can be no doubt from these changes that poliomyelitis is a general systemic infection. In perhaps no other disease is there such a close similarity between the human illness and that experimentally produced in monkeys. Not only the anatomical lesions but the clinical symptoms are identical.

This disease is best transmitted to monkeys by injecting the virus intracerebrally and the disease can be inoculated from one monkey to another. The studies made on these animals have proved that the causative factor is a virus and not merely a toxin and that pathologic changes affect the entire organism and are not confined to the spinal cord. Flexner and Amoss have shown recently that the virus is present in the tonsils and nasopharyngeal mucus in the early stages of the disease but cannot be detected after the second week. This confirms the clinical observations that after the paralysis or convalescence has set in the infectivity diminishes and that it is most contagious during the period of invasion as are nearly all of the communicable diseases of childhood.

Classification.—The first classification of any real value was made by Wickman who divided the cases into the following forms:

1. Spinal poliomyelitis
2. Resembling Landry's paralysis
3. Bulbar or pontine
4. Encephalitic
5. Ataxic
6. Polyneuritic (resembling neuritis)
7. Meningitic
8. Abortive

This is useful in clinical cases and describes the various types seen in practice. From a scientific standpoint it is not so valuable, as the pathologic findings do not always correspond with the clinical symptoms.

A number of writers have recommended classifications based on clinical, anatomic, pathologic or symptomatic manifestations. Holt and Howland, in the last edition of their book, use a very simple and yet comprehensive classification which meets the needs of the general practitioner. This includes:

    1. Spinal
    2. Bulbospinal
    3. Non-paralytic

They do not include the cerebral type which they feel is an encephalitis not necessarily due to the virus of poliomyelitis.

SYMPTOMS

Period of Incubation.—The incubation period in the experimental disease of monkeys shows a variation of from two days to two weeks. In human beings it seems to be somewhat shorter, usually under eight days. Wickman placed it from one to four days. In one case the onset was reported as appearing twenty-four hours after contact; in another as late as eighteen days. The average is from five to seven days.

Preparalytic Stage.—In the majority of cases the onset is sudden with all the symptoms of a general systemic infection. The severity of the critical symptoms, however, bears no relation to the subsequent course of the disease. The cases showing the most severe and acute symptoms at the onset may not be followed by severe involvement of the central nervous system. The reverse is also true and mild initial symptoms may be followed by extensive paralysis and even death. The temperature usually ranges between 101° and 103° F. In very acute cases it may rise to 105° F. In some instances the disease is ushered in by a convulsion, probably due to the high fever. This fever usually lasts for three or four days when it falls by crisis. A feeling of lassitude or drowsiness frequently accompanies the fever, although in a small percentage of the cases the brain seems more active and alert.

There is a general pain of hyperesthesia in most of the cases. It may be so severe that the slightest touch will cause pain. Attempt to move the arms or legs is accompanied with pain in some children, while in others it is general and spontaneous and the little patients cry most of the time. Headache is a constant symptom. The pains may be in any or all parts of the body but are most frequent along the spine and back of the neck.

If the head is bent forward the pain is intensified, causing the child to cry out and resist. This is considered an important diagnostic sign.

There are the usual gastro-intestinal symptoms accompanying fever and an acute infection. There is loss of appetite during the febrile stage. Vomiting is a frequent symptom and may be so severe as to suggest acidosis. Constipation is more often present than diarrhea. This constipation may be hard to overcome, especially if the abdominal muscles are affected.

The throat is usually congested, causing pain in swallowing. In many cases there is a coryza and running eyes. There is often a marked tendency to profuse sweating. This is not only present in the febrile stage but it may continue into convalescence. It may be limited to one part of the body, to one half of the face or to one extremity. Retention of the urine is not infrequent and its possibility should always be looked for.

Draper separates the clinical symptoms into four main groups. First, the abortive or non-paralytic cases, in which no paralysis follows the initial systemic disturbance. Second, those which have a period of well-being after the initial symptoms followed by another well-defined attack of illness. In this group the virus in the blood produces the signs of a general infection. It later gains entrance to the nervous system and paralysis and other nervous symptoms then develop. Third, those cases in which there is no intermediary cessation of symptoms and the symptoms of fever, etc., of the first phase drag over and fuse with those of the second phase. Fourth, those fulminating cases in which the secondary phase of the disease is the only one and the symptoms point to the virus attacking the nervous system immediately on its entrance to the body.

The paralysis or loss of power may come on quickly in the course of a few hours or, as is more frequently the case, it develops slowly and its extent is not known for three or four days. As long as there is any fever there is a great probability of the paralysis extending.

Paralytic Stage.—There is no symptom outside of the paralysis that indicates the onset of this stage. An analysis of seven hundred cases in the New York City epidemic of 1916 showed that 71 per cent of the cases showed paralysis before the fourth day. The longest interval between the initial symptoms and paralysis was twenty-one days.

This paralysis is sometimes very difficult to detect in young children and takes very careful searching to locate. It may be brought out by gently pricking the extremities with a pin. In older children who will coöperate it is easy to determine the extent and position of the paralysis. It may be only a loss of strength or a temporary weakness. It may be limited to a single muscle or it may be generalized.

The extent and distribution of the paralysis is well illustrated by the

following grouping of 868 cases occurring in the Swedish epidemic of 1905
as given by Wickman:

One or both legs...353
Combination of legs and arms...............................152
Arms and trunk.. 10
Ascending paralysis... 32
Whole body 23
Spinal and cranial nerves................................... 34
One or both arms... 75
Legs and trunk... 85
Trunk alone.. 9
Descending paralysis....................................... 13
Cranial nerves alone....................................... 22
Not given.. 60

Holt and Howland collected and grouped 550 sporadic cases from vari-
ous sources with the following result:

One leg..229
Both legs..176
Combination of arms and legs............................... 42
One arm only... 14
All extremities and trunk.................................. 79
All others... 10

The legs are involved in the great majority of cases in both groups,
while the infrequency with which the arms are involved is rather striking.
The legs receive their nerve supply from the sacral segments of the cord
which is the most vascular portion. Any muscle or group of muscles may
be affected. In the thigh the quadriceps femoris is most frequently para-
lyzed, while in the lower leg the anterior group of perineals, the flexors of
the foot and the extensors of the foot are most often involved. The
flexors of the toes are not commonly affected; because of the weakness of
the extensors, as well as the force of the gravity, there not infrequently
results the very common toe and foot drop.

The muscles involved most frequently in the upper arm are those of
the shoulder group, especially the deltoid.

Paralysis of the diaphragm is very serious and is the cause of most of
the fatal cases. When the diaphragm is affected the respiration is thoracic
and the abdominal wall is retracted instead of protruding during inspira-
tion. This usually develops quite late in the disease. The intercostals
are often involved with the diaphragm. These muscles are affected in as-
sociation with widespread paralysis of the arms and legs, in the rapidly
ascending types of paralysis and in the very severe infections. The respira-

tion is shallow and is an exaggeration of the normal infantile type. When they are involved at the same time as the diaphragm, there is absolutely no hope for recovery, the patient dying from suffocation.

The back muscles are not infrequently involved. Paralysis of one or both extremities is usually associated with it. It is easily overlooked in young children as they are not able to sit up in the acute stage. Later there are apt to be curvatures of the spine, especially a unilateral scoliosis.

Abdominal muscle paralysis is not uncommon and can be recognized, when the child cries, by a bulging or ballooning of the paralyzed section.

The types of paralysis outlined above result from involvement of the anterior horn cells of the cord and are included in the spinal type of poliomyelitis.

When the cranial nerves, pons and medulla are involved the cases are included in the bulbospinal type. This group, according to Wickman, forms only about 6 per cent of the cases. The onset does not differ from the spinal type of cases and the distinction is seen only after the paralysis develops. Any of the cranial nerves may be affected. When the third is paralyzed the pupil is dilated and does not react to the light. The facial is most frequently involved. This is easily determined by the symmetry of the face when the child cries. The facial paralysis is usually transient although it may be permanent. There is great difficulty in swallowing when the ninth nerve is affected. Hypoglossal paralysis often accompanies that of the facial nerve. When the pneumogastric nerve is affected the respiration becomes difficult and the heart action is accelerated.

The rare clinical type is called acute ascending or Landry's paralysis. It may be ascending or descending but in either case it involves the respiratory centers as well as causing difficulties in swallowing and speaking. It is rapidly progressive; usually only three or four days intervene before death relieves the patient. It is a distressing condition as the mind usually remains clear.

Another rare type is known as the ataxia form in which the child falls easily and there is a loss of equilibrium. There is usually no atrophy of the muscles. There may be a transitory disturbance of speech causing the child to stutter and have difficulty in enunciating. The lesions are supposed to be in the cerebellum, pyramidal tracts or in Clark's column.

Abortive or Non-paralytic Form.—Wickman divides the non-paralytic cases into four classes:

1. Those with the course of a general infection
2. Those showing meningeal irritation
3. Those with marked pains suggesting an influenza
4. Those with accompanying gastro-intestinal disturbances

These are the cases which do not show paralysis although some may present marked meningeal symptoms. They probably form the largest group in any epidemic and may comprise from 60 to 85 per cent of all cases. Their recognition has explained many points in the spread of the disease. There is nothing especially characteristic in the initial symptoms on which to base a diagnosis, which can only be made positively on laboratory evidence, namely, (1) the characteristic changes in the cerebrospinal fluid; (2) the successful inoculation of the disease into monkeys when the virus obtained in nasal and buccal mucous membranes is sufficient in amount; (3) the demonstration of immunizing principles in the blood such as are found in persons suffering from the disease and which are not found in normal blood.

The Cerebrospinal Fluid.—There are characteristic changes in the spinal fluid in the initial stage of the disease which are of the greatest importance in diagnosis. The fluid is under pressure. It is sterile and generally clear, although it may present a slight cloudiness. A slight fibrin web sometimes forms in it but not so constantly nor is the web as large as in tuberculous meningitis. The number of cells is definitely increased as are the albumin and globulin contents. While the normal fluid contains from five to ten cells per cubic centimeter, in poliomyelitis they are increased to between twenty and one hundred, in some cases reaching as high as five hundred per cubic centimeter.

During the onset of the disease the polymorphonuclear cell predominates and may form 80 or 90 per cent of all the cells. After the appearance of paralysis the type changes to mononuclear lymphocytes, which then form from 75 to 100 per cent of the cells. DuBois and Neal believe that large mononuclear cells of an endothelial type which are present are especially characteristic of poliomyelitis. The cells rapidly disappear from the spinal fluid so that after two weeks the cell-count may return to the normal. Fehling's solution reduces both the normal fluid, and that obtained during the course of the disease.

Reflexes.—When the paralysis is complete the deep reflexes are absent; in partial paralysis they are diminished. There are, however, many exceptions to this statement. The reflexes may be normal or they may be highly exaggerated and Babinski's sign present.

Blood.—This does not differ from any of the acute infections. There is a polymorphonuclear leukocytosis of from fifteen to sixty-five thousand. The blood chemistry is normal and there is no change in the non-protein nitrogen fractions.

Urine.—Care should be taken to see that there is no retention of urine. In the acute febrile stage there is very apt to be a small amount of albumin present but nephritis does not occur.

TABLE XXIX.—CEREBROSPINAL FLUID IN VARIOUS MENINGEAL CONDITIONS IN CHILDREN *

	Normal	Meningismus	Serous Meningitis and Encephalitis	Poliomyelitis, Polioencephalitis	Tuberculous Meningitis	Pyogenic Cerebrospinal Meningitis	Lues, Epilepsy
Color	Clear	Clear	Clear or opalescent	Clear or opalescent	Clear to opalescent	Cloudy turbid	Clear
Pressure	Comes in drops	Increased	Increased	Increased	Increased	Increased	Increased or normal
Quantity	Up to 10 c.c.	Increased	Increased	Increased	Increased	Increased	Increased
Clot formation	None	None to very slight	Early fibrin web	Early fibrin web	Fibrin web from coagulation	Clot	None
Fehling's	Reduced	Reduced	Reduction decreased	Reduction decreased	Tends not to reduce	Decreased or not reduced	Reduced
Nonne albumin	No increase	Usually no increase or very slight	Increase slight to 3	Increased especially late	Increased	Increased	May be either
Noguchi globulin	No increase	Usually no increase or very slight	Increase slight to 3	Increased especially late	Increased	Increased	May be either
Potassium permanganate	Index below 2	Around 2	Early 2 Late 2	Early 2.5	2.5 up to 5	3	
Bacteriology	None	None	None	None	T.B.	Specific	None
Fixation (biologic)	None	None	None	None			Wassermann
Cytology number	10-12	20	50-100	Early, very high, 1000	Late high 300	High	10
Polynuclears		80-100 per cent	Occasionally 50 per cent	Early 60 per cent 80-100 per cent	Acute high percentage 80-100 per cent	80-100 per cent	
Lymphocytes (small mononuclears)			800-100 per cent	Often high	Usually 90-100	Few	
Large mononuclears						Few	Few
Endothelial	Few	Few		Numerous	Small percentage	Occasional	Few

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* From *Abt's Pediatrics.* Courtesy W. B. Saunders Co.

DIAGNOSIS

There is more difficulty in reaching a diagnosis in sporadic or isolated cases than during an epidemic. During an epidemic the laity as well as the medical profession are on the alert and at such times there is but slight doubt that, between the professional and non-professional alertness, there will be included all cases which are poliomyelitis.

From a clinical study of the symptoms in the early or preparalytic stage it presents no characteristic signs other than those of a general infection. The chief aid in diagnosis is the spinal fluid. If it is increased in quantity, in cell-count, contains no bacteria, if globulin is increased and Fehling's solution is reduced, it could point to poliomyelitis. The general rule is that if the cell-count and the fluid are normal, poliomyelitis may be excluded.

The diagnosis in sporadic cases is usually not made until the paralysis has developed.

A history of exposure is suggestive, especially in the presence of an epidemic. The onset and course of the disease with its symptoms of general infection would exclude congenital and long-standing cases of brain and nerve diseases.

There may be some difficulty in differentiating between poliomyelitis and tuberculous meningitis. Poliomyelitis is more sudden and abrupt in its onset and the cerebral symptoms appear only a short time after the initial symptoms. No trustworthy diagnosis can be made without an examination of the spinal fluid. There is much greater pressure in tuberculous meningitis, the number of cells are larger and small lymphocytes predominate, and sooner or later there are changes in the eye-grounds which are never seen in poliomyelitis. There are many similarities at the onset with cerebrospinal meningitis but the meningococcus that can be found in the spinal fluid settles that point. The spinal fluid in acute syphilitic meningitis shows a positive Wassermann. Meningitis accompanies many inflammatory diseases such as pneumonia and ileocolitis, the presence of which would exclude poliomyelitis, but in these cases an examination of the spinal fluid would remove any doubt as to the diagnosis.

Facial or Bell's palsy may present difficulties in diagnosis, especially during an epidemic. Such a paralysis coming after exposure to cold or ear trouble, without any acute systemic symptoms and with a normal spinal fluid, points conclusively to Bell's palsy.

There are a number of surgical conditions, such as fractures, sprains and other injuries on account of which the child cannot move an arm or leg, which at first might suggest poliomyelitis. This is likewise true of paralysis or loss of power which comes from internal or external pressure on a nerve.

In all such cases the diagnosis should be withheld until the next day or after an examination of the spinal fluid has been made.

There may be a pseudoparalysis or a spasm in some of the nutrition disorders in children such as scurvy, rickets and tetany. A careful examination of the child as well as a study of the history of the attack should remove any doubt concerning the diagnosis. In scurvy there are swellings, hemorrhages from the gums, very acute hyperesthesia and a history of improper feeding.

Hysteria is rare in young children. The reflexes and spinal fluid are normal and there are marked sensory disturbances. If the paralysis exists for some time there is no atrophy of the parts involved such as is present in poliomyelitis.

PROGNOSIS

No definite prognosis can be made during the acute febrile stage. So long as fever is present there is a possibility of extension of the process. A child with very slight initial symptoms may develop a rapid ascending paralysis which will end fatally, while on the other hand a case with an acute onset may subside in a few days without any signs of paralysis. The cerebral cases are the less favorable and when the muscles of the diaphragm and the intercostals are involved the outlook is hopeless. The mortality in reported epidemics varies from 8 to 42 per cent of the cases. A low and a high mortality may occur in the same year in different parts of the same state or county.

The question of whether a paralyzed muscle or set of muscles will regain its function is important. Here the age of the patient seems to have some influence. The younger the child the more apt it is to have a restored function. Paralysis may appear on any day of the acute onset but it is safe after the seventh day to say that there will not be any paralysis. The recovery of paralysis and of function varies in different epidemics. The electri-

TABLE XXX.—DEATH RATE FOR POLIOMYELITIS PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1924, ACCORDING TO SEX

Year	Male	Female
1915	.5	.4
1916	39.6	27.9
1917	1.0	.8
1918	.6	.5
1919	.3	.4
1920	.6	.4
1921	2.8	2.2
1922	1.6	1.2
1923	1.3	.8
1924	1.8	1.5

TABLE XXXI.—DEATH RATE FOR POLIOMYELITIS PER 100,000 POPULATION OF THE UNITED STATES DEATH REGISTRATION AREA IN NEW YORK STATE FROM 1915 TO 1925

Year	United States Registration Area	New York State	New York City	New York State Exclusive of New York City
1915	1.0	0.5	0.2	0.7
1916	10.0	33.5	46.1	19.2
1917	1.6	0.9	1.0	0.8
1918	1.2	0.6	0.5	0.6
1919	0.9	0.3	0.3	0.4
1920	0.9	0.5	0.7	0.2
1921	1.8	2.5	2.5	2.5
1922	0.8	1.4	0.9	2.0
1923	0.9	1.0	0.9	1.1
1924	..	1.7	1.5	1.8
1925	..	1.9	1.7	2.1

TABLE XXXII.—DEATH RATE FOR POLIOMYELITIS PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1924, ACCORDING TO AGE

Age, Years	Number		Rate		Per Cent of All Cases	
	1915	1924	1915	1924	1915	1924
Under 1..............	7	14	2.9	6.0	.03	.1
1....................	9	19	4.8	8.9	.2	.6
2....................	3	16	1.5	7.3	.1	1.1
3....................	5	15	2.6	6.8	.4	1.6
4....................	3	19	1.6	8.9	.3	2.4
5-9..................	5	39	.6	3.7	.2	1.5
10-14................	2	28	.2	2.9	.1	1.5
15 and over..........	13	33	.2	.7	.01	.3
TOTAL ALL AGES ..	47	183	.5	1.7	.03	.1

cal reactions are of value in prognosis of muscle restoration. Muscles which soon lose completely their contraction to the faradic current rarely recover their function. A return of faradic contractility is a favorable sign and if this is not again lost, improvement can be confidently assured. The after treatment of the muscles has a very important bearing on the restoration of functions. Lovett has showed that with proper muscle training in the hands of an expert six times as many cases will recover as would be the case if treated by the older methods. There is great damage done by unnecessary meddling or aggressive therapeutics in the early stage of paralysis.

Recovery of muscle function may take place after the muscle has been helpless for six months. After a year the chances for spontaneous improvement are slight and after two or three years none at all.

PREVENTION

Every epidemic must start from an initial case; each sporadic case must be guarded and controlled as well as all contacts. It is easy to quarantine and limit the activities of persons ill with the disease; there is no way to control the unrecognized healthy carriers, of whom there must be many more than there are actual carriers.

Poliomyelitis in a locality causes great fear and much anguish to parents and neighbors. This is largely due to the popular belief that every child who contracts the disease will either die, or if fortunate to survive, will become a cripple for the rest of his days. This great dread led to hysterical methods of community control during the 1916 epidemic in the State of New York. Children under twelve were not permitted to enter a very large number of towns and cities, and policemen guarded the roads and railroad stations, holding up automobiles and making a farce of public health regulations. All this was fodder to the flame of fear and created a state of panic not justified by the disease itself. In large cities it is impossible to control the spread by such measures; but in small communities with a few cases a strict police quarantine can be kept over patients and contacts and this may have some effect in preventing the spread of the disease.

The problem of prevention is of greatest importance during an epidemic. Now that the nature of the virus is known, as well as its mode of entrance into and escape from the body, the methods of prevention are better understood. There is no doubt that infantile paralysis is spread by human beings through human contact, so the essential points are to control the original focus and isolate all contacts. The disease itself should be managed like any other communicable disease. In the presence of an epidemic every child or adult with an apparently simple cold should remain in reasonable isolation until it is over or until it is shown not to be infantile paralysis. The general rule among health officials is to isolate every case for three weeks from the date of onset of the disease. Children who have been near a patient must be kept under official observation for two weeks from the last date of contact.

The value of isolation during epidemics was well illustrated in New York City during the 1916 epidemic, when there were nearly nine thousand cases in the city. The Department of Health enforced a rigid quarantine in ninety-three institutions which cared for over twenty-one thousand young children, and no cases developed therein. At the United States Army post on Governors Island there were about ninety children whose fathers were officers or soldiers attached to the post. No children were admitted to the island or permitted to leave from July 4 until the end of September, and not

a single case of poliomyelitis developed among these children. On the island there is an excellent water supply and sewage disposal system, the surroundings were ideal and the standard of living high. In contrast to these conditions were those on Barren Island, where all of New York City's garbage is taken for disposal. Here there were about three hundred and fifty children under sixteen years of age. The standard of living was of the lowest, and rats, mosquitoes and flies abounded. There was no sewer system and surface wells furnished the water supply. But a strict quarantine was maintained by the health department during the epidemic and no cases of infantile paralysis occurred.

The proper disposal of discharges from the nose, throat and bowels not only of the patient but of all in isolation is of great importance in preventing the spread of the disease. Soiled handkerchiefs and clothing should be immediately boiled.

The use of antiseptic sprays for the nose does more harm than good, as they do not destroy the virus and do have a tendency to injure the mucous membrane. It has been shown that the nasal secretions themselves are destructive to the virus, and such action would seem to be best promoted by no interference.

TREATMENT

Acute Stage.—The essential and most important treatment in the acute stage is rest—*absolute rest*. This is as necessary in the mild as well as the severe cases. The child must be put to bed as soon as the diagnosis is made, or before if there is fever, and kept there until the inflammatory processes have subsided even though this may last for several weeks. The child must not be allowed to leave his bed, for every movement increases the congestion in the spinal cord and causes action on the part of the motor cells which should be kept at rest to permit the greatest amount of repair work to go on.

The pain and tenderness so distressing in many cases can best be relieved by this absolute rest. It has been found that in cases of extensive paralysis, placing the limb or body in a plaster jacket or cast does much to relieve the suffering.

Such casts should be cut at the end of two weeks in such a way as to permit the body or limb to be lifted out, rubbed, bathed and then replaced. This procedure should be repeated as long as any tenderness is present even if it continues two or three months. During this period there should be no manipulation, electricity or massage. Changes of position are desirable and there is no objection to outdoor air. Immersion in hot water and attempts to make active movements under water should be encouraged.

The paralyzed limb can be kept in position with the aid of sand or salt

bags. Heat is often welcomed and the bags may be heated or the limbs wrapped in flannel and external heat applied.

Anodynes may be necessary. A combination of codein and antipyrin is often useful. Some of the barbituric acid derivatives, such as allonal, or amytal, relieve the pain without any disagreeable after effects.

Special care must be taken to prevent bed-sores. Sponging with alcohol and a free use of talcum powder with circular pads to relieve the direct pressure are of help.

Lumbar puncture is indicated not only as an aid in diagnosis but also as a therapeutic aid. In cases of the meningeal type where there is an increase in the intracranial pressure the relief after the fluid has been withdrawn is very striking. The procedure should be repeated as often as the pressure symptoms become evident.

There are no specific drugs in this disease. Some writers recommend hexamethylenamin in large doses in the early stages, but others have not seen any benefit. Indiscriminate drugs will do more harm than good.

Serum.—Flexner and Amoss and other authorities demonstrated that the virus of poliomyelitis could be neutralized or rendered inert in monkeys by the action of serum taken from recovered cases. As a result of these experiments a serum from recovered patients was injected intraspinously in a large number of cases in the 1916 epidemic. The conclusions reached were not entirely convincing, but the serum seemed to exert a protective influence if injected during the first twelve hours of the acute onset.

The serum is obtained by bleeding a recovered case and separating the serum and adding a small amount of tricresol to preserve it. A lumbar puncture is made, as much fluid as will run out of the needle is removed and about half as much of the serum is made to flow back into the spinal canal. Amoss feels that the use of this serum intravenously is of benefit.

The acute symptoms, such as headaches, fever, general malaise, etc., seem to be aggravated after the serum injection, but there appears to be much proof that the use of this serum in large quantities both intraspinously and intravenously does prevent paralysis.

Rosenow, of the Mayo Clinic, has prepared an antistreptococcus serum which he and others claim is specific. This position is not yet endorsed by many observers and further work must be done in a large number of cases before its value can be established.

Other Treatment.—There is nothing special to be said regarding the diet, except that a light diet is indicated during the febrile stage. The kind of food to be given is largely what, within reason, appeals to the patient. It is necessary to feed by gavage when the muscles of deglutition are involved. Rectal feedings may be employed in these cases.

There is very little to be done when the muscles of respiration are paralyzed. Oxygen gives relief and the child should be encouraged as much as possible as the mind is usually clear and alert.

The bladder must be emptied by catheterization at regular intervals when there are disturbances of the bladder muscles.

Metzer at the time of the 1916 epidemic claimed excellent results from hypodermic injections of adrenalin chlorid and his work has received corroboration from other physicians. He felt that adrenalin would overcome the edema and other inflammatory processes surrounding the nerves and relieve congestion.

FIG. 18.—POLIOMYELITIS.
Nurse showing mother how to give muscle exercises prescribed by orthopedic surgeon.

The technic is to remove some of the spinal fluid and inject in its place 2 c.c. of a 1:1,000 solution of adrenalin every six hours from the beginning of the disease. When the injections are started early in the disease the subsequent paralysis is said to be lessened and recovery is expedited. These results have not been verified by later investigators.

Convalescence.—This period, which occurs from the fourth to sixth week after the onset, may be said to commence when all tenderness has left the affected muscles. The period extends until the muscles have recovered their function or until two years have elapsed. During this period the child should be under medical supervision. The parents should not become discouraged but should coöperate in every way in encouraging the patient to

take his exercises and other measures to restore the strength of the affected muscles.

The time for active muscle treatment dates from the disappearance of tenderness. Even if this occurs before the fourth week it is advisable to wait until that time so that the general physical health of the child has been restored.

Massage.—Massage may be used in this stage and is a most valuable method of treatment. It possesses several advantages. The general nutrition is improved by the passive exercise of the muscles which will also prevent their atrophy and deterioration. It causes an increased flow of

FIGS. 19 AND 20.—POLIOMYELITIS.

The little girl in Figures 19 and 20 was stricken with infantile paralysis when four months old. From that time until brought to the after-care clinic of the State Department of Health, when eight years old, her only method of locomotion was by hitching along, holding her left ankle on the ground, by which method she obtained leverage to pull herself forward (Fig. 19). On the advice of the orthopedic surgeon she was sent to a hospital for an operation. Six months after the operation braces were applied and since that time with their aid she has been able to walk (Fig. 20). The power of some of the paralyzed muscles has gradually increased.

blood and lymph to and from the affected muscles, thus hastening the removal of the waste products of metabolism. Massage should not be overdone or the treatment continued long enough to cause overfatigue of the muscles. The age and condition of the child must be carefully considered. Giving the massage under water in a warm bath tends to increase the flow of blood and makes the exercises easier.

Heat.—Where the circulation of the paralyzed limb is sluggish the hot air bath is often advisable and desirable before massage, for the heated muscle acts more easily. A simple method of providing heat is by means of the electric heating pad. Moist heat from hot, wet towels is of value, but

as high a temperature cannot be obtained as well as dry heat and it may irritate the skin.

Electricity.—This formerly was the most popular method of treating paralysis. It should not be employed to the exclusion of other measures. Used unintelligently it does more harm than good.
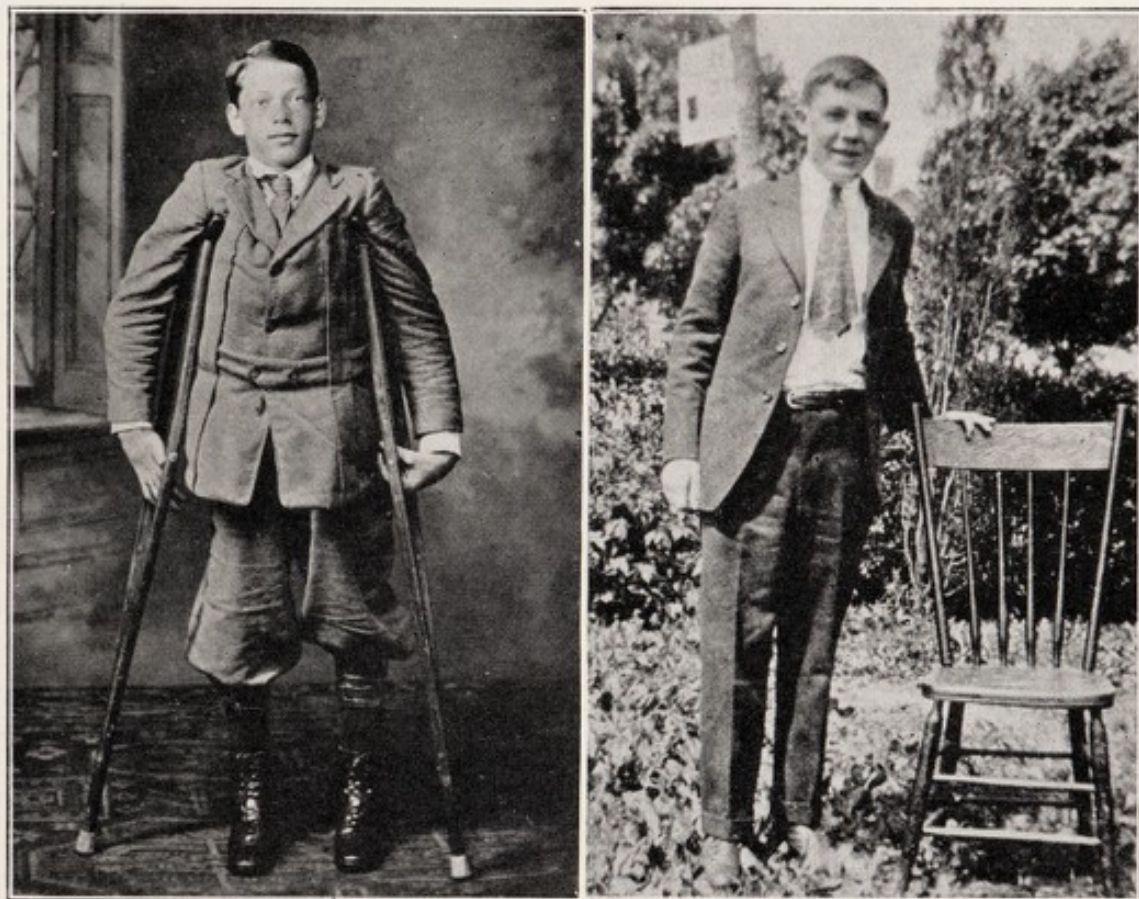
FIGS. 21 AND 22.—POLIOMYELITIS.

M. W., sixteen years of age, was attacked with poliomyelitis in the fall of 1916, just as he was about to enter college. When seen at the first clinic in December, both legs and back were paralyzed. Instructions given at the clinic were followed faithfully and conscientiously by the patient and his mother, who, under the direction of the nurse, learned muscle training. For a time he wore braces and a support to his back, but in September, 1918, he was sufficiently recovered to discard his braces and back support and reënter college with lessened physical difficulties. This boy will probably ultimately become practically normal.

Either the galvanic or faradic current may be used but the confidence of the child must not be lost through using too strong a current. The faradic current should cause the muscle to contract. The positive pole should be placed over the muscle and the negative pole applied to the spine. A very weak current may be used at the first treatment and gradually increased. If the muscle does not respond to the faradic current there is no use in continuing. The physician or nurse should always test the current themselves before applying to the child.

Muscle Training.—This is the most modern method of treatment and is without doubt the most valuable, but it must be carried out by nurses who have received special training and instruction. It aims to establish new connections between the brain and the affected muscle. Lovett, who worked out this method, defined it as an attempt to aid the patient to perform a certain movement with the hope of stimulating an impulse from the brain to the selected muscle. For example, if the dorsal flexors of the foot are paralyzed the foot is dorsally flexed by the hand and the patient directed to assist. If there is any muscular response the aid given by the operator is gradually lessened and in time the muscles can be trained to perform their function. Any one who desires further information of the method of muscle training is referred to Lovett's *Treatment of Infantile Paralysis* and Wright's *Muscle Training in the Treatment of Infantile Paralysis*. A deformity must be corrected before treatment of any kind can be successfully instituted. It is much better to prevent a deformity than to cure it, and this can often be accomplished by careful and appropriate treatment in the early stage of the disease.

Fatigue and overuse of the muscles during this stage must be avoided. Muscles can atrophy from too much as well as too little use. Lovett suggested the use of a spring balance by which the strength and pull of the muscle can be measured. The results should be recorded on a chart and the treatments adapted accordingly. Muscles partly paralyzed but in which power is returning can be rendered functionless by even slight grades of non-use.

PUBLIC HEALTH REGULATIONS

Infantile paralysis is a communicable disease and as such must be reported at once to the local health officer and is subject to the rules and regulations of the health department. The New York State Department of Health requires strict isolation of such cases with removal to a suitable hospital. No person except the physician, nurse or other person in attendance is permitted to come in contact with or to visit such a case. All articles coming into contact with discharges from the nose, throat and ears of the patient shall be disinfected and destroyed. The sick room and premises shall be thoroughly cleansed when the patient is released. The minimum period of isolation in New York State is three weeks from the day of the onset of the disease.

The patient is not allowed to return to school until twenty-one days from the date of onset. Other children, if the patient remains at home, cannot return to school until fourteen days after the quarantine has been raised, if nonimmune. If immune a child is excluded until one week from termination of quarantine or removal from quarantined premises.

If the patient is removed to a hospital or other children leave home when the disease is discovered, the children must be kept out of school for two weeks from date of removal. Other children who have been exposed to the so-called contacts if not immune, are excluded from school two weeks from date of last exposure.

The American Public Health Committee has summarized our present knowledge of poliomyelitis as follows:

1. INFECTIOUS AGENT.—A filterable virus of undetermined morphology.

2. SOURCE OF INFECTION.—Nose, throat, and bowel discharges of infected persons or articles recently soiled therewith. Healthy carriers are supposed to be common.

3. MODE OF TRANSMISSION.—By direct contact with an infected person or with a carrier of the virus, or indirectly by contact with articles freshly soiled with the nose, throat, or bowel discharges of such persons, and probably by drinking milk contaminated by the nose, mouth and bowel discharges of persons in the active stage of the disease.

4. INCUBATION PERIOD.—Uncertain because of inexact information as to period of communicability and essentials for exposure, but believed to be from three to ten days, commonly six days.

5. PERIOD OF COMMUNICABILITY.—Unknown; apparently not more than twenty-one days from the onset of disease, but may precede onset of clinical symptoms by several days.

6. METHODS OF CONTROL

    (*a*) The infected individual and his environment

        1. *Recognition of the Disease.*—Clinical symptoms, assisted by chemical and microscopical examination of the spinal fluid.

        2. *Isolation* of all recognized cases for three weeks from febrile onset.

        3. *Immunization.*—None.

        4. *Quarantine* of exposed children of the household and of adults of the household whose vocation brings them into contact with children, or who are food handlers, for fourteen days from last exposure to a recognized case.

        5. *Concurrent Disinfection.*—Nose, throat, and bowel discharges and articles soiled therewith.

        6. *Terminal Disinfection.*—Cleaning.

    (*b*) General measures during epidemics

        1. Search for and examination of all sick children should be made.

        2. All children with fever should be isolated pending diagnosis.

        3. Education in such technique of bedside nursing as will prevent the distribution of infectious discharges to others from cases isolated at home.

CHAPTER XIV

EPIDEMIC ENCEPHALITIS

Definition.—Epidemic encephalitis is an acute, infectious disease, due to a specific virus, characterized anatomically by widely disseminated lesions in the central nervous system, particularly in the midbrain, and manifested clinically by a variety of symptoms, but most constantly by fever, lethargy or somnolence and ophthalmoplegia.

Synonyms.—Encephalitic lethargica, nona.

HISTORY

The literature regarding epidemic encephalitis dates from 1917 when von Economo described an epidemic in Vienna of lethargic encephalitis in which the diagnostic criteria consisted of somnolence, ophthalmoplegia and profound asthenia. During the stress of war conditions von Economo presented a study of the pathological and clinical manifestations of a disease entity, hitherto unrecognized, which later reports have served only to amplify and confirm. In the following year epidemics occurred in France, England and the United States and later were reported from widely separated areas. These epidemics presented a new disease to the physicians practicing at that time, but in the light of present studies it is possible to interpret certain obscure epidemics of previous times and scattered case reports in literature as epidemic encephalitis. Particularly is this true of the *Schlafsucht* which occurred in Tübingen in 1712-1713 and a disease called *nona* which appeared in Italy in 1889-1890. In both of these epidemics lethargy was a prominent feature, but their extent and severity was not comparable to that of the present period.

A disease which is so grave, so obscure and so varied in its manifestation has naturally evoked intensive study in this age of research with the result that from a zero point of knowledge previous to 1917 there has grown an imposing mass of scientific data to which more is constantly accruing. Particularly are the postencephalitic phenomena receiving the attention of the neurologists, psychiatrists and psychologists as the years elapse since the onset of the disease.

Early studies of the disease attempted to identify it as an atypical form of anterior poliomyelitis and also to establish a connection between it and

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influenza. The best scientific opinion is now opposed to both of these positions and the arguments pro and con are not presented here.

ETIOLOGY

The causative organism of epidemic encephalitis is unknown. The febrile course of the disease, its pathological anatomy, and its occurrence in epidemic form leave no doubt as to the infectious character of the disease, but the mode of infection is obscure. There is also reason to believe that the disease exists in endemic form. Contact infection is rare. Two cases of the disease in the same family are reported in less than 1 per cent of cases.

Experimental studies to date present conflicting evidence. Loewe and Strauss have isolated a filtrable virus which produces encephalitis in monkeys and rabbits with lesions characteristic of the disease. They have been able to pass the virus through many series of animals although about 50 per cent of rabbits are immune to encephalitis. On the other hand, other investigators have failed to isolate the virus and have found stock rabbits which have not been inoculated which present the pathological picture of encephalitis. It has further been found that the virus from herpes simplex produces results identical with those of the virus from epidemic encephalitis. As long as the causative organism is unknown and its characteristics not fully understood the mode of conveyance of the disease cannot be determined. A life history is needed. The clinical course of the disease with its periods of quiescence and recrudescence suggests that like the virus of syphilis it is capable of returning to activity from time to time.

Route of Infection.—Until there is evidence to the contrary it is a fair assumption that the virus of epidemic encephalitis first infects the upper respiratory passages from whence it passes on to infect the brain. While there is no definite catarrhal stage associated with its early manifestations, a sore-throat is frequent. In view of the frequency of an initial conjunctivitis the virus may possibly pass from the eyes to the brain.

Age.—No age escapes infection. Cases on record include the newborn infants in the first year of life, and even one case which died of epidemic encephalitis at eighty-four years of age. Neal found one-half of her one hundred cases were under fifteen years, but Wechsler found that the greatest number of his cases fell between the years twenty to fifty. His tabulation:

Cases of Epidemic Encephalitis	Below 5 Years	6-10 Years	11-20 Years	21-30 Years	31-40 Years	41-50 Years	51-60 Years	61-70 Years	Over 70 Years	Total
Number	13	37	136	222	215	140	72	23	6	864
Per Cent	1.5	4	15.7	25.7	25	16.2	8.3	2.8	.7	100

Ass. Research Nerv. & Ment. Dis., 1921.

Seasonal Incidence.—The seasonal incidence of epidemic encephalitis is rather definitely confined to the winter months. The curves of incidence reach their peaks in January, February or March and show a decided falling off by June. This is of interest in comparison with poliomyelitis which is essentially a disease of the summer months.

Sex.—American statistics show males are affected more frequently than females in a proportion of 3 to 2, but the records of the British Ministry of Health show males and females in equal numbers in all age periods.

Predisposing Causes.—All occupations and all stations of life are represented in case reports. Parsons found that about seven-tenths of his cases followed indoor occupations and only one-tenth outdoor occupations. The other two-tenths fell in an indeterminate class. From this he concludes that the disease chiefly attacks those who spend the greater part of their day in indoor occupations. It is interesting to note that Wechsler found 2 per cent of the cases in his group were physicians, which in comparison to the number of physicians in the general population makes the incidence about sixteen times as great. In a recent study Browning was able to elicit a history of prolonged lack of sleep in twenty-eight cases which succumbed to infection. Upon this ground he explains cases that follow school examinations and the high incidence among physicians. Exhausting influences of any kind probably play a contributary rôle.

PATHOLOGY

Despite the varied clinical manifestations of epidemic encephalitis, the pathological findings are fairly consistent.

Gross Appearance of the Brain and Spinal Cord.—The macroscopic findings are slight—a congestion of the superficial vessels, both large and small, impart a pink color, and free blood may be seen in the sulci. Minute hemorrhages occur but massive hemorrhages into the piæ are rare. The pia arachnoid may be edematous. The dura mater in general shows no lesion. The congestion, when it extends to the spinal cord, fades out as it recedes caudally.

The cut surfaces of the brain show corresponding signs of congestion. The vessels are everywhere prominent and minute hemorrhages impart a mottled appearance. The lesions are most intense in the midbrain, pons and medulla, least in the cerebellum. The gray matter shows more changes than the white. The tissue is uniformly softer than normal. The ventricles are normal in size and contain spinal fluid unaltered in appearance.

Microscopic Appearance.—*Perivascular infiltration* is a constant and characteristic phenomenon. The vessels chiefly affected are the small veins, but the larger veins, arteries and capillaries may be involved. In extent the

infiltration varies from a single layer of cells partly surrounding the vessel to a complete sheath formed of many layers of cells which contribute a striking feature to the histological picture. The cuff extends for a varying distance along the course of the vessel. The infiltrating cells are large and small mononuclear lymphocytes and plasma-cells. The infiltration is largely confined to the Virchow-Robin and perivascular spaces. The gray matter of the basal ganglia, midbrain, pons, medulla and spinal cord suffers the greatest changes, but the white matter does not entirely escape.

In the same regions and frequently in connection with the perivascular infiltration is found a diffuse infiltration of the nerve tissue. The same type of cells is seen with an occasional large mononuclear phagocyte. This infiltration is usually described as most intense in and near the substantia nigra.

Hemorrhage is usually microscopic and confined to the perivascular space of His. It is not associated with marked vascular disease.

Nerve Tissue and Neuroglia.—The nerve-cells show a relatively small amount of degeneration considering the severity of the pathological process. Generalized degeneration or focalized degenerations of large extent have not been described but lesser degrees of degeneration, as cell destruction, eccentricity of the nucleus and chromatolysis, occur. Neuroglia cell proliferation is considerable in the regions of intense cellular invasion. The reaction of the *meninges* is slight.

The pathological picture varies in degree rather than in special characteristics in the various types of the disease.

LABORATORY FINDINGS

Blood.—The blood offers no diagnostic criteria. The red blood-cells remain unchanged. The leukocytes may be increased to 20,000 or may show no increase. Blood cultures are sterile.

Urine.—There is a slight increase in albumin, such as might be expected in an infectious disease.

Spinal Fluid.—The spinal fluid is usually clear, under some increase of pressure. The Wassermann is always negative. The cell-count is usually increased to ten or fifteen cells, predominantly mononuclear in type. The sugar is not increased. The colloidal gold chlorid curve is frequently altered but in no characteristic manner. The spinal fluid may be entirely normal.

SYMPTOMS AND CLINICAL COURSE

Prodromata.—Epidemic encephalitis has the prodromata common to all general infections and, in addition, its own peculiar characteristics. The onset may be sudden or may be preceded by several days of malaise with

symptoms resembling those of influenza—general malaise, headache, fever, drowsiness with periods of restlessness or delirium, particularly at night, are common.

Gastro-intestinal symptoms as vomiting, or less frequently diarrhea, may mark the onset. *Difficulty in urination* may be the first symptom. *Drowsiness* usually increasing is encountered. *Diplopia* is an important early symptom. It may precede, accompany or follow the drowsiness. *General prostration* is often the first complaint. *Mental symptoms* as delirium, mania or confused states may usher in the attack. In children a sudden outbreak of extreme naughtiness or talkativeness may mark the beginning of encephalitis. *Severe neuralgias,* particularly in the abdominal region, are sometimes the first disturbance.

General Symptoms.—*Fever* is usually present at some time, usually moderate in degree and of short duration. It may be absent or it may be extremely high. A steadily rising temperature before death is not uncommon.

Headache often of great severity may be present during the acute state of the disease. It is usually persistent and is not affected by the ordinary analgesics.

Lethargy is frequent, in fact so frequent that it has given one of the names to the disease. It varies in different epidemics, in different patients and in the same patient from time to time. The sleep may be so deep that the entire period of its duration may be a blank, but more characteristically it is a drowsiness from which the patient can readily be aroused to answer questions. Recovered patients sometimes report that they were conscious of their surroundings but were unable to arouse themselves. The desire for sleep may be so irresistible that the patient falls asleep while engaged in some activity. The duration of the lethargy is variable. It may last for days or weeks and it may disappear to return even after the lapse of months. Lethargy may be absent throughout the course of the disease. Various theories have been advanced as to the cause of the lethargy, as increased intraventricular pressure, interference with afferent paths, disordered hypophyseal function and poisoning of psychic synapses by the virus.

Insomnia and Nocturnal Excitement.—The association of wakefulness and delirium at night, with somnolence by day, is a characteristic and pathognomonic feature especially in children. It is more than mere wakefulness, for the child is positively and pathologically excited. The activity brings about exhaustion which results in sleep during the following day. The child awakes rested and is fairly normal until the easily fatigued brain is again tired when the excitement returns. This feature may occur early in the disease or may be delayed seven or eight weeks after the onset. It may persist and become a troublesome residuum.

Symptoms of the Nervous System.—*Ocular disorders* of some kind have been a feature of all the epidemics. Conjunctivitis is frequently noted. Disorders of motility are particularly common. All the disturbances to which the pupils are subject have been recorded in encephalitis. Nystagmus is frequent.

Disorders of the different cranial nerves lead to disturbances of their functions. Dysphagia is fairly frequent.

Mono-, para- and hemi-plegias are reported from time to time.

The condition of the deep reflexes is variable. Myoclonus, sometimes painful but more often painless and hardly noticed by the patient, is often a part of the clinical picture. The distribution of the jerks is varied but most commonly the upper half of the abdominal sheet of muscles is involved.

Chorea-like movements are characteristic of some epidemics. Choreo-athetotic movements and tremors are encountered. Convulsions resembling those of epilepsy may be an early or late symptom.

Mental disturbances are frequent and of great variety. Delirium has already been referred to and acute mental states occur. In the beginning the patient is almost always irritable and later extreme apathy is frequent. Great talkativeness is a striking feature in children in the beginning. Often they are the victims of extreme depression.

Other Symptoms.—*Gastro-intestinal disturbances* are largely incidental to the general infection. Constipation is often obstinate and persistent. The mouth is usually foul and excessive salivation may be seen.

The skin frequently presents a rash but it is so variable in character as to be of little aid in diagnosis. Severe sweating sometimes occurs. Cases of herpes zoster have been reported.

TYPES OF THE DISEASE

The varied manifestations of encephalitis have led to numerous classifications as to types. As the type of involvement has little influence upon the management of the case and is dependent upon the nerve-cells involved, the simplest classification is the most useful. The one by MacNalty follows:

Type I.—In which there is a general disturbance of the functions of the central nervous system but without localization.

Type II.—In which in addition to general disturbance there are various localizations in the central nervous system:

 1. Clinical affections of the third pair of cranial nerves

 2. Affections of the brain stem and bulb. Local lesions of other cranial nerves

3. Affections of the long tracts
4. Probable involvement of the cerebellar mechanism
5. Affections of the cerebral cortex
6. Types indicating some evidence of spinal cord involvement
7. Types indicating possibly an affection of peripheral nerves

Type III.—Mild or so-called abortive cases.

Epidemic hiccough is considered by some a distinct type of epidemic encephalitis.

SEQUELÆ

Alterations of the mental state as sequelæ of epidemic encephalitis form one of the most serious problems connected with this disease. Mental disturbances such as changes or alterations in character, disposition or behavior are more common in children than in adults. Behavior oddities and even criminalistic tendencies are frequent in the young. Pierce Clark says that definite changes in disposition and behavior result when the disease attacks a child's developing brain, whereas an attack in an adult tends to a more physical expression of the inflammatory process such as the paralysis agitans syndrome and abnormal involuntary movements. These mental changes show great variability which suggests that epidemic encephalitis may disturb any mental function. Among the changes may be mentioned bad temper, incorrigibility, hysterical attacks, insomnia, moral perversity such as lying, stealing, cruelty, profanity, etc., loss of memory and fears and phobias of all types. It is a great problem how to deal with these cases. They are not mental defectives and they are not insane. Parents should never punish children with these disorders. They should be given plenty of rest and should be humored as far as consistent. It is best to keep them out of school and away from other children, as they are apt to provoke trouble and invite combat with their playmates.

Dawson and Conn made a study of the intelligence quotient (I. Q.) of forty-six encephalitis cases on a basis of a series of Binet tests at intervals ranging from a few days to five years after the onset of the disease. Their conclusions are of great interest. They found the average intelligence of these forty-six children was significantly lower than that of 974 other hospital patients and of their own brothers and sisters. This mental deterioration is due to arrested mental development and the younger the child the more severe it appears.

The so-called parkinsonian syndrome sometimes appears as a sequela in children. This is a condition characterized by expressionless face, monotonous voice, stiff shuffling gait with short steps and head fixed and looking straight ahead with arms motionless and hanging by the side of the body.

Dawson and Conn found that postencephalitic children with parkinsonian syndrome showed a deterioration in intelligence not significantly different from that of other patients.

DIFFERENTIAL DIAGNOSIS

Epidemic encephalitis must be differentiated from cerebrospinal meningitis, cerebral abscess, cerebral tumor, tuberculous meningitis, cerebral syphilis, the cerebral forms of poliomyelitis, typhoid fever with hebetude, lead encephalitis and coma from various causes. The multiplicity and diversity of symptoms make the diagnosis of epidemic encephalitis difficult. Lethargy, ocular palsies and elevation of temperature suggest encephalitis, but a differential diagnosis often must be made by a process of exclusion. The findings of the laboratory in the blood and spinal fluid, close observation and the procession of the symptoms must all be considered.

Cerebrospinal Meningitis.—In this the course of the disease is more rapid, the spinal fluid is cloudy, shows a marked cellular increase, particularly of polymorphonuclear leukocytes, meningococci, both intra- and extracellular, and is under increased pressure.

Cerebral Abscess.—History of a severe injury or long-standing suppurative otitis media or mastoiditis, or fulminating sinus disease with a hectic fever and leukocytosis suggest the diagnosis of brain abscess. Increased cell-count in the spinal fluid and a relative bradycardia are also suggestive.

Cerebral Tumors.—Differential diagnosis of brain tumor and encephalitis involves the question of surgical intervention. In the absence of fever and with evidence of increased cranial pressure with headaches and vomiting there is indication for operation although a similar group of symptoms may occur in encephalitis.

Tuberculous Meningitis.—The onset is insidious, the temperature rises toward the end and the disease terminates fatally. The spinal fluid shows a gradually increasing number of cells, upon standing produces a characteristic pedicle and by guinea-pig inoculation the tubercle bacilli may be recovered. Meningeal symptoms are prominent.

Cerebral Syphilis.—This is excluded by serological tests. The Wassermann is always negative in the spinal fluid of encephalitis and positive in that of cerebral syphilis. The stupor is continuous and the patient when roused fails to answer intelligently, while in encephalitis the patient can be aroused and responds to questions.

Poliomyelitis.—In its typical form poliomyelitis is easily distinguishable from encephalitis but if the medulla or pons are principally involved the diagnosis is more difficult. Factors to be considered are: The seasonal

incidence of poliomyelitis, its predilection for childhood, the presence of meningeal symptoms and the evidence of frank paralysis with subsequent atrophy and the reaction of degeneration. Lethargy is rare.

Other Conditions.—*Typhoid fever with hebetude* is excluded by a positive blood culture or a positive Widal reaction.

In *comatose states* there is a total loss of reaction to sensory stimuli.

Lead and metallic encephalopathies are rare conditions in children. Peripheral palsies, abdominal palsies, a lead line and changes in the red blood-cells fix the diagnosis. The spinal fluid shows a heavy globulin reaction.

PROGNOSIS

A prognosis either as to the immediate or ultimate outcome is uncertain and should be given with caution. There is great variation in the character of the epidemics and the degree of involvement in the individual cases. It must always be regarded as serious. The mortality rate is probably about 20 per cent, and of those who survive about three-quarters carry sequelæ. Those cases which have an acute onset with the development of severe toxemia, marked delirium, high fever, coma and myoclonic features are most apt to have a fatal termination.

Sequelæ may appear months or years after the original infection. The parkinsonian syndrome does not usually improve, in fact it tends to grow progressively worse. The behavior disturbances show improvement in many cases. The disturbance of sleep may eventually lessen or disappear even after existing for years. The mental states except when actual defect occurs show improvement or recovery, although it may require many years for its accomplishment.

TREATMENT

There has been discovered as yet no specific drug or serum treatment for epidemic encephalitis. The treatment is symptomatic. Absolute quiet and rest in bed are of extreme importance and if possible the child should be removed to a hospital. Nurses should be in constant attendance. The room should be well ventilated and kept rather dark as photophobia is present in most of the cases in the early stage. Although the patient may be in a state of lethargy he may be easily aroused and excited and restless by any noise. He should not leave the bed and a bed-pan must be used. The bladder should be watched so as to prevent overfilling. The use of a catheter may be necessary. Sponging the body occasionally is desirable but too frequent bathing is to be avoided on account of disturbing as well as exerting the patient. The diet should be fluid during the acute stage. If the child is in stupor forced feeding may be indicated. If he does not take enough fluid and

dehydration develops, hypodermoclyses and intravenous injections of normal salt solution or 10 per cent glucose solution are necessary.

The use of auto or convalescent serum both intraspinously and intravenously has been recommended by some clinicians who claim satisfactory results, but they have not been used extensively enough to demonstrate their value.

Hydrotherapy in the form of cold packs or cold sponging is useful in reducing the restlessness and delirium. If it is necessary to give drugs, 5 to 10 grains of sodium bromid with 3 to 5 grains of chloral every two or three hours. Antipyrin and phenacetin are useful drugs in this condition especially if there is much headache. In cases of delirium and marked mental excitement prompt relief will be obtained by the hypodermic use of hyoscin hydrobromid in doses from $\frac{1}{100}$ to $\frac{1}{150}$ grain repeated in two hours if necessary. Lumbar puncture has not only diagnostic value but a decided therapeutic value. It can be repeated every twenty-four hours during the acute stage if the spinal fluid pressure is increased, but after the acute stage it is of little value.

The insomnia is often very troublesome and if sponging and other simple measures are not effective it may be necessary to resort to drugs. It is safe to administer veronal, adalin, etc., in small doses or allonal in 2-grain doses. Luminal alone or combined with sodium bromid is an effective hypnotic.

The eyes are often inflamed and bathing with a 4 per cent solution of argyrol or a 2 per cent solution of mercurochrome is of value in the more severe cases. When double vision is present it is a good plan to keep one eye covered with a patch.

The hygiene of the mouth should receive careful attention. The mouth, teeth and tongue should be cleansed after each feeding. A weak solution of listerine, lavoris or boric acid is suitable for this purpose. The lips and tongue should be kept moist and may be gently rubbed with albolene. An ice-bag can be applied around the throat if the glands are swollen.

Constipation is often a troublesome feature and requires attention. Mild laxatives or mineral oil may not be sufficient and it is often necessary to administer large doses of saline cathartics each morning. An ounce of warm mineral or olive oil injected in the rectum at night to be retained until the next morning is of value in softening the stool.

Tympanites is frequent in the early stages and can be relieved by hot turpentine stupes, simple diet and measures for the relief of constipation. The insertion of a rectal tube may be necessary if the gas is in the lower colon. The hypodermic use of 1 c.c. of pituitary extract is an excellent remedy when the distention is marked.

Convalescence.—Great care must be taken to prevent the child from entering too soon into his normal activities. Rest and plenty of it is of prime

importance. These postencephalitic children are very easily fatigued both in mind and body. The child should remain in bed until all acute symptoms and signs of progressive nervous and mental involvement have subsided. At first he should only get up for a very short period, which is gradually lengthened, and if any signs of fatigue appear placed in bed again. This need for a long and protracted rest cannot be overemphasized. When possible a prolonged convalescence in the country should be secured for the child as the mental and nervous sequelæ sometimes develop months after the child is apparently well.

Mental rest is as necessary as physical rest and these children must not be excited by visitors, playmates, exciting stories, moving pictures and the like.

PUBLIC HEALTH REGULATIONS

This disease has been recognized only in the past ten years, but in spite of its varied manifestations the Sanitary Code of the State of New York includes it in the list of communicable diseases which must be reported to the health department. The status states, "it shall be the duty of every physician to report to the local health officer, within whose jurisdiction such patient is, the full name, age, and address of every person affected with epidemic (lethargic) encephalitis within twenty-four hours from the time the case is first seen by him." The attending physician has to give detailed instruction to the nurse or other person in attendance, instruction as to the disinfection and disposal of discharges from the nose, mouth and ears of the patient. The health officer is obliged to post a placard stating the existence of the disease "on the house or apartment or room or rooms in which such case is isolated, near the entrance thereof."

Children of the household where this disease exists are excluded from public, private or Sunday schools until permitted to return under the rules of the local health authorities.

CHAPTER XV

CEREBROSPINAL MENINGITIS

Cerebrospinal meningitis is a specific infectious disease, caused by the *Diplococcus intracellularis meningitidis,* which occurs sporadically or in epidemics. It is characterized anatomically by inflammation of the cerebral and spinal meninges, and clinically by an irregular febrile temperature, various nervous and meningeal symptoms and often by petechial or purpuric eruptions.

Terminology.—The commonly employed term "epidemic cerebrospinal meningitis" is misleading in view of the many sporadic cases which occur in all of the large cities. The most specific and descriptive term is meningococcus meningitis, since it designates the etiological factor. The older literature describes the disease under the terms of spotted fever, spotted typhus, black fever, brain fever, epidemic cephalalgia and cerebrospinal fever.

History.—The classical history of cerebrospinal meningitis was written by Hirsch in 1885. He classifies the epidemic prevalence of the disease in four main periods, while the epidemics of the twentieth century may be considered to constitute a fifth period.

The *first period* begins in 1805 with an epidemic on Lake Geneva. The pathological findings of Mathey in this epidemic establish the identity of the disease without question. It is not conceivable that it was a new disease at that time and earlier epidemics described under the names of cerebral fever, petechial fever and cephalalgia may well have been meningococcic meningitis, but lacking postmortem evidence they cannot be distinguished positively from typhus and other malignant fevers. In 1806 a vivid picture of the disease is given by Danielson and Mann in an article entitled, "A Singular and Very Fatal Disease which Lately made its appearance in Medfield, Mass." From this time until 1830 it occurred in the United States and in scattered epidemics in Europe.

During the *second period,* 1837 to 1850, the disease prevailed in widespread epidemics in the military centers of France, Italy, Denmark, Algiers and the United States.

The *third period,* 1854 to 1875, found the disease disseminated through most of Europe, Western Asia, the United States and parts of Africa and South America.

A *fourth period,* which lasted from 1876 to 1886, yielded isolated epidemic outbreaks in various portions of the world.

The *fifth period* may be considered to have dated from 1896 and to be in existence at the present time. It is to this period that we owe our most notable progress in combating the disease. Two great epidemics, one in New York in 1904-1905 and one in Prussia in 1905-1907, despite the most improved methods of treatment showed a mortality as high as in the earlier epidemics. But the brilliant achievement of Flexner, whose first publication appeared in 1906, in producing an effective serum, marks an epoch in the history of the disease.

BACTERIOLOGY

The meningococcus, or *Micrococcus intracellularis meningitidis,* belongs to the group of Gram-negative cocci, all of which, with the exception of the gonococcus, may be found in the nasopharynx of healthy people. The members of the group are:

1. Meningococcus
2. Gonococcus
3. Micrococcus flavus
4. Micrococcus catarrhalis
5. Micrococcus pharyngis siccus
6. Diplococcus mucosus capsulatus

The meningococcus is about 1 micron in diameter, being larger than the gonococcus, but smaller than the *Micrococcus catarrhalis.* It is non-capsulated. When obtained from the spinal fluid of an infected case they closely resemble the gonococci. They are found both intra- and extra-cellularly, usually in pairs but sometimes in tetrads. The definite flattening of the adjacent edges gives them a kidney-bean appearance. Variation in size of the cocci in the same smear of spinal fluid is a noticeable feature and of some diagnostic importance. In cultures also variation in size occurs. An excess of extracellular organisms indicates a severe infection. It is non-motile and non-spore-bearing.

Staining Reactions.—The meningococcus stains easily with the usual aqueous aniline dyes. It is invariably Gram-negative when the method is carefully carried out. The Leishman stain colors the meningococcus blue and brings out the characteristics of the cells, hence it is useful in cellular reactions during the course of the disease. In an established case of meningitis the polymorphonuclear leukocytes contained in the first spinal fluid are usually degenerated and stain poorly, but as the patient improves fresh leukocytes appear which stain well. In cases of meningitis the organisms are usually readily found upon examination of the spinal fluid, but in subacute cases and those examined late in the disease a prolonged search may be necessary in order to find them.

Cultivation.—The meningococcus grows readily upon meat-infusion culture-media, but the growth is more luxuriant and rapid upon media to which animal proteid in the form of blood-serum or ascitic fluid has been added. For cultivation directly from the human body it is advisable to smear the surface of the culture-medium with a few drops of human blood and to plant in rather large quantities (1 to 2 c.c.), since many of the cocci fail to produce colonies. Of the various media which have been used, "tryp-agar" has been found one of the most valuable. This trypsin broth legumin agar was perfected by Gordon and Hine as a result of their studies of the cultural characteristics of the meningococcus. If it is enriched by 2 per cent of ascitic fluid or horse serum the stock cultures may be kept alive for several weeks.

For blood cultures, 10 c.c. of the patient's blood, taken at the height of the paroxysm of fever, is added to 50 c.c. of ordinary bouillon. Growth appears on the second or third day as a very slight turbidity.

The meningococcus is an obligatory aërobe and lack of oxygen is almost inhibitory to growth.

The optimum temperature is 37° C., although growth will take place at temperatures ranging from 25° to 42° C. Failure to grow at 23° C. is considered of some diagnostic importance.

Viability.—Outside the human body the meningococcus has a short life. It is sensitive to heat and cold and is especially susceptible to drying. In daylight at room temperature the organism usually dies within an hour, but if moisture is present it may live for two hours or longer. It is killed by ordinary disinfectants in high dilution on short exposure. Normal saliva inhibits the growth of the meningococcus, but this property appears to be proportional to streptococci contained in the saliva, as nasal mucus has no inhibitory effect.

Agglutination.—Immunization of animals by repeated inoculations of meningococci results in the formation of agglutinins in the blood-serum. By means of agglutination tests Gordon and Murray in 1915 differentiated four main groups or "types" of meningococci. Gordon found that the majority of these nasopharyngeal organisms can be identified with some one of these types, but a group which he terms "pseudo meningococci" have no affinity for the types previously classified and form a group by themselves. Worster-Drought and Kennedy found that each of their cases of cerebrospinal meningitis yielded only a single type of meningococci and that the type of the meningococcus that was present in the nasopharynx of the patient at the onset of the disease was always of the same type as that obtained from the spinal fluid when that was positive.

Complement Fixation.—Experiments with the complement fixation test have proved to be of less value than the results obtained by agglutination.

Toxin.—The meningococcus elaborates an endotoxin by which it produces its deleterious effect. This is liberated by the autolysis of the organism. Cultures of the organism sterilized by heat readily kill susceptible animals while filtered cultures do not.

Pathogenicity.—Animals are not very susceptible to infection by the meningococcus. Subcutaneous inoculation results only in a local reaction unless large quantities are used. White mice are the most susceptible of the laboratory animals. In these an intraperitoneal inoculation gives rise to peritonitis from which the animal usually dies. The peritoneal exudate shows meningococci. Guinea-pigs and rabbits are less susceptible and very large intraperitoneal doses are necessary to produce a fatal result.

Meningitis is not produced by intravenous or intraperitoneal injection of the meningococcus, nor does the introduction of the organism into the nasopharynx produce meningitis. Flexner, introducing the organisms intrathecally in monkeys by means of lumbar puncture, has produced a meningitis which is pathologically similar to that in man.

DISSEMINATION OF THE DISEASE

The contagiousness of cerebrospinal meningitis is slight but positive. Only a small proportion of those exposed to infection contract the disease and usually only one case occurs in a family. This is probably a matter of individual immunity, for the majority of people are not susceptible. In epidemics the disease spreads irregularly and many times no connection between the cases can be traced.

All persons who contract the disease have the meningococci in the nasopharynx at some stage. Failure to secure it from cultures is due to the low viability of the organism which is particularly susceptible to drying and to cold. A refined technic is therefore essential to secure positive cultures. Repeated investigation of contacts has shown that a large proportion of them become carriers, harboring the organism in the nasopharynx, where it lives as a saprophyte though capable of producing the disease should it enter the throat of a susceptible person. These carriers are probably themselves immune to infection as few of them develop the disease.

Carriers may be classified as temporary and chronic. In the temporary carriers the organism may be found upon one examination, while swabs taken later at frequent intervals are negative. Worster-Drought and Kennedy in observing 140 carriers found that ninety-five were temporary and forty-five were chronic. The chronic carriers harbored the organism for varying periods up to eighty days, although the duration in the majority of cases was from a week to a month.

The spread of infection may occur in any of the following ways:

1. From a case to an individual who develops the disease
2. From a case to a person who becomes a carrier
3. From a carrier to another person who becomes a carrier
4. From a carrier to one who develops the disease

Investigators have reported that from 7 to 70 per cent of contacts become carriers. Considering the low viability of the meningococcus it is safe to consider as contacts only those who have come in intimate association with the patient within a closed building. Flügge found that 70 per cent of those in close proximity to a case of cerebrospinal fever became carriers. He estimates that the number of carriers is from ten to twenty times as great as the number of cases that occur at a given time.

The number of carriers among healthy persons, non-contacts, has been the subject of frequent investigation. It is found to vary with the season of the year, a decided diminution taking place during the warm months.

All the present evidence is in favor of the direct spread of the meningococci from throat to throat, particularly inside buildings, such as schools, houses and theaters, where a warm saturated atmosphere allows the organism to be borne in the air without drying. This may occur as a droplet infection in coughing, sneezing, and emphatic talking, but is not likely to occur in quiet conversation. Infection may also be acquired by direct contact as in kissing, but is unlikely to be spread by contaminated clothing and utensils because of the rapid destruction of the organism under unfavorable conditions.

The presence of carriers in a community explains the disconnected manner in which most cases occur. Chronic carriers serve to keep the organism alive from season to season and from one epidemic to another.

ETIOLOGY

Predisposing Causes.—Cerebrospinal meningitis is essentially an epidemic disease, hence certain factors which may affect a considerable number of persons must exist in addition to the presence of a virulent strain of the meningococcic organism in order to produce a rapid rise in the number of cases. Some of these may be enumerated:

1. *Climatic Conditions.*—Climate alone is not responsible for the disease as it has been reported in almost every part of the world. Sudden and marked variations in temperature, which are particularly frequent in temperate climates where meningitis most commonly occurs, probably act to weaken the resistance of the individual. Children have a relatively greater body surface to become chilled, a factor which may have a bearing upon their greater susceptibility.

2. *General Hygiene and Overcrowding.*—In cities the disease is more prevalent among the poorer classes living in crowded dwellings. Its frequency in overcrowded barracks is noteworthy. The explanation is that in crowded quarters persons are in close contact with the carriers and the air which is saturated with moisture is favorable to the life of the meningococci as they are sprayed from the throats of the carriers. Cool air and drying bring about their destruction.

3. *Age.*—The disease has been considered by continental writers as affecting particularly children and soldiers. Children have less resistance than adults, due in part, as suggested above, to the variation in body temperature. The resistance of soldiers is lessened by fatigue. Their concentration in large numbers in camps and the shifting character of the population bring them in contact with a larger number of carriers than is the case in civilian life.

4. *Previous health* seems to play but a small part in susceptibility as the disease attacks persons of the most robust constitution.

5. *Catarrhal conditions* may predispose to susceptibility to the organism.

Incubation Period.—For many of the exanthemata the incubation period is a definite interval between the time of the entrance of the organism and their multiplication to sufficient concentration to produce a reaction in the body. In the case of the meningococcus in many instances after it gains access to the throat it remains merely as a saprophyte which, after an indefinite time, is lost, although from it many others may have become infected. As the carriers in general do not develop the disease it appears that for those affected the incubation period is short. Evidence collected by Worster-Drought and Kennedy led them to conclude that: "Carriers may develop the disease at almost any time up to six or seven weeks after infection . . . such observations do not afford evidence of the duration of the true incubation period. . . . It would appear that the incubation period varies between twenty-four hours and seven days, its average duration being nearly four days."

Mode of Invasion.—The portal of entry for the meningococcus is the nasopharynx. From there its mode of extension to the meninges is probably either direct or by way of the blood stream. Most of the evidence is in favor of the latter method.

Infection by the Blood Stream.—According to this view the organisms multiply in the nasopharynx, are absorbed in the blood and are carried thereby to their site of election, the pia arachnoid. Clinical evidence favors this view, particularly as the meningococci can be obtained in blood cultures in the premeningitic stage of the disease. Herrick states that positive blood cultures can be obtained in from 50 to 80 per cent of cases examined in the early stages. Worster-Drought and Kennedy cite a case in which the blood

culture was positive for meningococci, while the spinal fluid was still clear and yielded no organisms either upon culture or microscopic examination. In many cases of the fulminating type death appears to be due to the overwhelming blood infection, while the postmortem examination shows the meningitis to be comparatively slight. In most cases the septicemia is of short duration and entirely disappears after the invasion of the meninges.

Infection by Direct Extension.—The possibility of infection of the meninges by direct extension of the nasopharynx is inferred from anatomical structure rather than clinical evidence. Extension by way of the middle ear is ruled out, as acute otitis media is rare in cerebrospinal meningitis and when it occurs it is as a complication late in the disease. The sphenoidal sinus has been suggested as a possible route. A sphenoidal sinusitis has occasionally been found but is by no means the rule and is considered to be secondary to the meningitis. Transmission through the ethmoid has been inferred on account of the communication between the lymphatics of the nose and the subarachnoid space. The virus of acute poliomyelitis has been found to pass in this way, but experimental proof is lacking for the invasion of cerebrospinal meningitis through the ethmoid to the meninges. Meningococci introduced into the nasopharynx in monkeys do not produce the disease.

PATHOLOGICAL ANATOMY

During the acute stage of cerebrospinal meningitis the essential pathological process is one of purulent inflammation of the arachnoid and the pia mater. The earliest lesions are seen in the region of the dilated blood-vessels at the base of the brain. Here an intense polymorphonuclear infiltration occurs. Then leukocyte infiltration becomes general in the meninges of the brain and cord. In time it extends the whole length of the cord, although the exudate is usually more marked in the cervical and lumbar regions. It may extend to the vertex of the brain. The subarachnoid space becomes filled with the exudate and large masses of coagulated material form partitions which interfere with the flow of the spinal fluid. In the chronic cases inflammatory adhesions cut off the fourth and lateral ventricles which become markedly distended from lack of drainage of the spinal fluid. In this exudate meningococci are usually abundant, both as intracellular and extracellular organisms. In the beginning the predominating cells are polymorphonuclear leukocytes but lymphocytes and red blood-cells are present in varying proportions. In addition there are found large cells from two to eight times the size of a leukocyte with a large extracellular vesicular nucleus and a granular protoplasm which contains smaller ingested cells. These arise from the connective tissue cells of the meninges. In the meninges themselves the organisms are less abundant and less often found ingested by the poly-

morphonuclears, which suggests that this phagocytic action takes place freely only after the meningococci are free in the subarachnoid space. The ventricular walls and the brain and cord cells immediately adjacent to the meninges become edematous; scattered leukocytes are found in the cerebral cortex and particularly in the cerebellum. Perivascular infiltration occurs both in the brain and the cord. In the latter the region of the posterior horn cells is particularly affected.

With the progress of the inflammation the cells of the exudate undergo degeneration, the large cells disappear and the lymphocytes and plasma-cells become abundant.

In chronic cases degeneration of the myelin sheaths and the posterior nerve roots may occur.

Extension of the inflammatory process may take place along the arachnoid sheath of the cranial nerves. The gasserian ganglion is often found imbedded in pus at an early stage.

The postmortem *macroscopic appearance* varies considerably with the type of the infection. In the acute fulminating type there is an intense injection of the leptomeninges and their normal transparency is lost. In the sulci a small quantity of turbid fluid is usually seen on the convexity of the brain. At the base there is often a small collection of pus. In cases of less severity in which death has occurred in from five to ten days the exudate is abundant, is yellowish green, thick and gelatinous. It is most abundant at the base of the brain and in the sulci of the convexity. A layer of pus may cover the upper and lateral surfaces of the frontal lobe and the anterior half of the parietal lobes. The membranes of the cord show corresponding changes. The ventricles are dilated and filled with a turbid fluid. The ependymal lining and choroid plexus are dull gray.

Cases which come to autopsy after a still more chronic course show a general thickening of the meninges in place of the exudate. Dense adhesions and opaque bands are seen. The ventricles usually show marked dilatation and pus is often present on the dependent portions after it has entirely disappeared from the surface of the brain.

The *other organs* show less significant pathological changes. The muscles and tissues are generally dry and the viscera show cloudy swelling. The spleen shows some softening of the pulp and some enlargement. Peyer's patches and the mesenteric glands are commonly swollen and in acute cases the intestinal mucosa is hemorrhagic. Pericarditis is occasionally present and, like malignant endocarditis, may be primary and occur without meningitis. Meningococcic pleurisy and bronchopneumonia may occur as complications. In cases with a rash, hemorrhages and leukocytic infiltration may be demonstrated in the skin. In the fulminating type the *adrenals* show hemorrhages. With prolonged retention of urine, cystitis may be present.

The *blood* shows an early leukocytosis (from 15,000 to 40,000 cells) which gradually falls as the case becomes chronic. A positive blood culture can be obtained in the fulminating type of the disease and in those cases which show a hemorrhagic rash. In other cases the organisms are in the blood but a short time and have usually disappeared by the time the symptoms are well established.

SYMPTOMS

The Onset.—The usual onset is sudden with headache, fever and vomiting. At the beginning the symptoms appear like ordinary influenza but the rapidly increasing severity of the illness suggests meningitis within twenty-four hours. The symptoms may so suddenly advance that in an hour or two the patient is comatose or delirious. In young children and occasionally in adults the onset is marked by convulsions. The vomiting is explosive in character and without accompanying nausea. Diarrhea instead of vomiting is encountered often in children but more rarely in adults. In children hyperesthesia is an early and prominent symptom. The trilogy of hyperesthesia, diarrhea and bulging fontanel is strongly suggestive of cerebrospinal meningitis.

Following the onset the symptoms fall into two groups, those due to general infection and those due to the involvement of the central nervous system.

Headache is a constant symptom, often of great severity at the onset and continuing throughout the course of the illness. Increased headache is frequently the first symptom of a developing internal hydrocephalus. With recovery the headache gradually disappears. The primary headache is probably due to the initial infection, later it is due to the increase in intracranial pressure which accompanies the increase in spinal fluid. It is frequently relieved by lumbar puncture.

Catarrhal symptoms in the form of sore-throat, coryza or cough may precede the onset by a few days or by a few weeks, in fact these may predispose to cerebrospinal meningitis. A bronchial catarrh may occur during the course of the disease without giving rise to physical signs in the chest.

Gastro-intestinal Symptoms.—The *tongue* first shows a whitish fur; later it becomes dry and brown.

Vomiting not preceded by nausea and explosive in character is a frequent symptom of the onset. This is usually limited to one or two attacks, but may continue for two or three days. It is a less frequent symptom in infants than in older children and in adults. In cases developing internal hydrocephalus the vomiting becomes projectile in character and very hard to control. If not relieved by lumbar puncture it is a grave sign. Vomiting may occur with a recrudescence of fever after a period of pyrexia.

Constipation is the rule as with other febrile conditions.

Diarrhea at the onset is frequent in infants and young children, but is rare in adults. Abdominal pain is usually associated with diarrhea.

The Temperature.—The course of the pyrexia is irregular throughout the course of the illness and is of small value as an index of the severity of the case. Following an initial chill with subnormal temperature there is a rapid rise, often to 103° or 104° F. In the fulminating type some die without ever exhibiting a pyrexia, while in the mild cases the rise in temperature is only slight. A considerable fall, often to normal, usually follows the first evacuation of turbid cerebrospinal fluid. In many cases after the first week the temperature remains at 100° F. or below. The fever usually terminates by lysis. In acute cases nearing death a rapid rise of temperature to 106° to 107° F. is not unusual. This may be due to a paralysis of the heat regulating center of the brain.

Pyrexia persisting after the termination of the meningitis, as evidenced by a clear cerebrospinal fluid, may be due to a complication, but in many instances it occurs without any discovered cause. During convalescence the temperature is unstable. Temporary elevation without any assigned physical cause may occur during the three or four weeks following the disease.

Cardiorespiratory Symptoms.—The *pulse* may be rapid at the onset, but with the development of symptoms the rate rapidly falls and is usually slow in proportion to the temperature. This bradycardia associated with pyrexia forms an important diagnostic feature. The *heart* clinically is frequently unaffected. The respiratory rate is usually only slightly quickened. It is seldom affected by lumbar puncture and the withdrawal of cerebrospinal fluid. In cases that end fatally death often occurs from respiratory failure while the heart continues to beat for an appreciable time.

Rashes.—Rashes are more common in adults than in children and their occurrence varies in the different epidemics. The cutaneous rashes accompany or closely follow the onset of the disease. They appear on the first or second day and are comparable to the rose spots of typhoid fever. In cases which show labial herpes there is usually an interval of two or three days between the appearance of the rash and the vesicles.

The characteristic rash is hemorrhagic and may be either small and petechial or purpuric. The petechiæ are not of grave significance but the purpuric areas are characteristic of the fulminating cases.

The rose spots, papules and petechiæ are probably embolic in origin and are evidence of the invasion of the blood stream by the organism. They are apt to occur at parts exposed to friction, especially at the joints. The purpuric rash is an intense form of the petechial. It consists of dark purple spots in size varying from that of a dime to a dollar.

Herpes labialis occurs with varying frequency in different epidemics and

usually appears on the fourth day of the disease. It is infrequent in children and exceptional in infants. Herpes zoster is less frequent than herpes labialis.

The Urine.—Albuminuria, glycosuria and hematuria may occur, but the organism is usually not present in the urine.

Symptoms of the Nervous System.—*The Mental Condition.*—Nervous symptoms predominate at the onset of meningitis and vary with the severity of the infection and the age of the patient. Severe headache is a feature almost constant in its occurrence and probably accounts for the very frequent insomnia. The mental condition is often one of delirium, even to the point of mania, alternating with drowsiness and apathy. In infants and young children the delirium is replaced by extreme restlessness and hyperesthesia. This may give way to drowsiness. In mild cases the mind may remain clear.

The Special Senses.—A striking and interesting feature of the eye symptoms is their variation from day to day. The disease may be ushered in with a photophobia but it develops more frequently in tuberculous meningitis than in cerebrospinal meningitis. This and conjunctivitis occur in about 10 per cent of cases. A certain degree of conjunctival congestion is very common and there may be conjunctival hemorrhages. These are important diagnostically since they rarely occur in other forms of meningitis. True nystagmus is present only in severe cases and is of grave prognostic significance since it is indicative of internal hydrocephalus. Strabismus, conjugate deviation and ptosis are all possibilities. Retraction of the upper eyelids when it occurs is the result of hydrocephalus.

The ear may be involved by the extension of the inflammation along the eighth nerve, causing deafness. In some cases this is permanent. Tinnitus aurium often is an early symptom of the disease. Otitis media may be a complication.

The Reflexes.—The condition of the reflexes is varied. *Kernig's sign* is practically constant and appears early in the disease. This consists of the inability to extend the leg on the thigh when the thigh is at a right angle to the trunk. It can be easily demonstrated by flexing the thighs on the abdomen when the patient is in a horizontal position in bed and then attempting to raise the legs to a position of complete extension. When present, reasonable attempts to extend the legs will fail. The condition is almost always bilateral and may persist for some time after the other symptoms have disappeared. This sign, of great significance in diagnosis in children above two years of age, is practically useless below that age because in normal infants there is often a physiological myotonia which may yield a positive Kernig's sign.

The cutaneous reflexes are usually increased but the tendon reflexes show no consistent variation. The Babinski toe reflex is often positive in meningitis but it is also normally positive in infants.

Muscular twitchings are sometimes observed. Convulsions may mark the onset of the disease.

The usual decubitus is lateral with the thighs flexed upon the abdomen and the legs upon the thighs. In extreme cases, especially in young children, the head may be thrown so far back that the occiput rests upon the shoulders.

CLINICAL TYPES

Fulminating Type.—This type of cerebrospinal meningitis is comparable to the malignant types of other specific infections. It is more frequent in some outbreaks than in others and may occur sporadically. It is seen less often in infants and young children than in older patients and occurs at the beginning rather than at the end of an epidemic. The patient is suddenly stricken, sometimes without warning, and death may take place within twelve to twenty-four hours. The usual symptoms are a chill, severe headache, stupor, extreme prostration, and coma. Delirium is usually present. A purpuric eruption of rapid development is practically constant. Autopsy shows hyperemia and opacity of the membranes, but generally no pus as the patient has succumbed to the overwhelming septicemia before there has been time for pus formation. Meningococci are found in the blood but the spinal fluid is frequently negative. Hemorrhages into the adrenal medulla, often found at autopsy, may account for the extreme prostration. The proper treatment is the intravenous injection of serum in large quantities.

Ordinary Acute Form.—Cases vary from the mild to the fulminating types. The ordinary case has an acute onset and after a short interval meningeal symptoms appear, including rigidity of the neck, violent headache, positive Kernig's sign and coma if the case is unrelieved by treatment. A prompt remission of symptoms results from effective energetic treatment, but recrudescences may occur. If treatment is begun late or is ineffective these cases become chronic from the formation of adhesions with a resulting obstruction of the ventricles and hydrocephalus.

Abortive Type.—In these cases the symptoms develop and subside rapidly with a duration of from two to six days. This type occurs more frequently at the end of an epidemic.

The patient becomes progressively more apathetic and may lie for hours without moving, with eyes open and staring. He may give an occasional cry. Food is taken greedily but vomiting, sometimes projectile in character, is often troublesome. Diarrhea may occur. The emaciation becomes extreme.

The temperature is irregular. During the first week it may range from 101° to 103° F., but later it remains near the normal level with occasional wide excursions. Just before death elevation again occurs.

Lumbar puncture at first yields a fair amount of cerebrospinal fluid which

contains meningococci and polymorphonuclear leukocytes. As the condition becomes chronic the fluid becomes scanty and contains only mononuclears. Dry taps are frequent, owing to the blocking of the foramen of Magendie and to adhesions blocking off the ventricles. Ventricular puncture performed during life yields the organism.

The course of this type of meningitis is essentially chronic. Lees and Barstow in thirty cases show an average duration of seven to eight weeks. It may continue for many weeks or even months. The mortality is over 75 per cent. In cases of recovery permanent blindness, mental impairment or deafness are frequent sequelæ.

The pathologic anatomy of this type differs from the ordinary adult type in that the seat of inflammation is at the posterior part of the base of the brain. The cisterna magna is filled with a yellow fibrinopurulent exudate. From here it spreads downward along the posterior aspect of the cord, inward toward the ventricles and forward along the base of the brain as far as the optic chiasm. The ventricles are almost always dilated and filled with clear or turbid fluid.

Posterior Basic Type of Infants.—This terminology is given to the chronic meningococcal infection occurring in infants, which, owing to the characteristics of infancy, presents a typical picture that before the days of diagnostic lumbar puncture was considered a clinical entity. The condition was first described by Gee and Barlow in 1878 under the name of cervical opisthotonos in infants. In 1898 Still demonstrated the identity of the infecting organism with the meningococcus of Weichselbaum.

It occurs both in epidemic and spasmodic form and is seen most often in children between the ages of four months and two and one-half years, but it may occur in children up to five years.

The *onset* is usually sudden with fever, vomiting and a convulsion or screaming. The characteristic retraction of the head occurs after a lapse of a few hours up to four or five days. This feature is so striking that the diagnosis may be made by inspection alone. With the head retraction is associated an opisthotonos which may be so marked as to draw the head back to the sacrum. The child bulges anteriorly while the abdomen is rigid and retracted. There is extreme spasticity of the limbs, the position of which is often in rigid extension with clenched hands and adducted legs.

The fontanels, when open, are tense and bulging. In young infants there may be a wide separation of the sutures and dilatation of veins of the scalp due to the increase of fluid in the ventricles. The pupils are dilated and a retraction of the upper lids gives the patient a peculiar staring expression. Strabismus occurs in the later stages of the disease and blindness of central origin is a frequent symptom.

Chronic Type.—These cases begin as the ordinary form but the course of the disease is protracted over several months. They are marked by irregular paroxysms of fever, alternate remissions and recrudescences of nervous symptoms and extreme emaciation. The chronic course may be due to (1) ineffectiveness of treatment—either the case has not been treated promptly or the serum has not been of the appropriate type so that the infection continues unabated—or (2) the cases have developed meningococcic adhesions which interfere with the free flow of spinal fluid and form closed cavities to which the therapeutic serum does not have access. In cases of obstruction to the flow of spinal fluid, lumbar puncture may yield only a small amount of clear fluid while the symptoms are clearly those of internal hydrocephalus. Death occurs from increased intraventricular pressure rather than from the infection. If recovery follows it is seldom complete, and leaves the patient with permanent sequelæ, either mental or nervous. The encysted or loculated form of spinal meningitis probably included the posterior basal meningitis of infancy, but it is here considered separately, as has been the custom of many writers.

LABORATORY FINDINGS

The Blood.—A polymorphonuclear leukocytosis is a constant finding. As a rule it is over 20,000 and it may rise to 40,000 or 50,000. In chronic cases the leukocyte count may fall to normal toward the end of the disease.

The Urine.—No characteristic changes are found in the urine. Cystitis may occur but the incidence of a pyuria varies with different epidemics. The infecting organism may be either the *Bacillus coli,* or the meningococcus. Albumin in the urine, if present, is in small quantities and has no prognostic significance. Hematuria and glycosuria are both rare.

The Spinal Fluid.—Normal spinal fluid is a clear colorless liquid with a specific gravity of 1.007-1.008 and a faintly alkaline reaction, contains few cellular elements—one to seven lymphocytes to the cubic millimeter and an occasional epithelial cell. There is a free circulation between the subarachnoid space and the ventricles. The work of Dandy, Blackpan, Dixon and Haliburton shows that the spinal fluid is secreted by the choroid plexus and that it is eventually absorbed by the blood stream through a process of diffusion and further that the flow from the blood stream to the spinal fluid is negligible. The normal pressure of the spinal fluid varies with several factors including age and position, but for practical purposes it may be considered that the normal flow from the lumbar puncture needle is one drop in two to three seconds.

In cerebrospinal fever the *pressure* of the spinal fluid as measured by the manometer is increased from the normal of 60 to 150 millimeters of water

to 650 to 1,000 millimeters of water (Worster-Drought and Kennedy), with the average in the neighborhood of 300 millimeters. The total amount of spinal fluid bears no constant relation to the intrathecal pressure.

The chief factor in the increase of this pressure is probably the hyperemia of the choroid plexus from inflammatory changes induced by the invasion of the meningococcus. No increase in pressure is found in the premeningitic stage (Worster-Drought and Kennedy) but a considerable increase is shown in cases punctured for the first time on the second day of the disease. Pressure of 600 millimeters or more is seen only in acute cases.

Quantity.—In normal persons lumbar puncture seldom yields more than 20 c.c. of spinal fluid, while 10 c.c. is the average amount. The amount in children is increased proportionately. In cerebrospinal fever the amount that may be obtained is distinctly increased. Patients punctured within twenty-four to forty-eight hours of the onset often give 80 to 100 c.c. of purulent or turbid fluid, and infants of one year may discharge from 20 to 30 c.c. Later in the disease the increase is less marked, while toward the end the amount lessens as the fluid becomes progressively more purulent, until finally only a few drops can be withdrawn. When the channels are blocked and hydrocephalus develops the spinal fluid diminishes until "dry taps" result.

In *appearance* the fluid varies from clear to turbid or purulent. Turbid fluids are most often seen in the first tap. Cases of moderate severity show more tendency to purulence upon the second tap than the first but tend to become clear with recovery. Chronic cases tend to become clear before recovery occurs and this is particularly the case in the posterior basic type of infancy. Fluids stained with blood are usually so because of rupture of a small blood-vessel either by puncture, if at the beginning of the flow, or by release of pressure upon the capillaries in the subarachnoid space if at the end. This has no significance. In a few cases of the acute type the fluid may be uniformly hemorrhagic, which is a grave indication.

The *proteins* are increased throughout the disease and may be demonstrated in the supernatant fluid after the cells have been removed by the centrifuge. A delicate fibrin coagulum forms within two hours after standing and occasionally a large coagulum will form almost immediately.

Glucose which will reduce Fehling's solution is a normal constituent of spinal fluid. This is lost during cerebrospinal fever but reappears with recovery. In the presence of hydrocephalus its reappearance has no prognostic significance.

Cellular elements are increased in all inflammations of the meninges. In meningococcic meningitis the increase is in polymorphonuclear leukocytes which are increased in large amounts as well as a smaller number of large and small lymphocytes and an occasional endothelial cell. Except in the fulminating type of cases in which death occurs before the inflammatory reaction is

well established the gravity of the case is proportional to the increase of poly-morphonuclears in the fluid. At the first puncture the leukocytes seem de-generate and stain poorly, but with improvement and probably as a result of the reaction to the serum treatment fresh and healthy leukocytes appear.

Bacteriology.—The positive diagnosis of cerebrospinal fever depends upon the demonstration of meningococci in the spinal fluid. With a refined technic it is possible to find them in practically all cases, although in the fulminating type the patient may die while the organisms remain few in number. In general there is a parallel between the severity of the case and the number of organisms present. The disappearance of the meningococci and particularly their failure to grow in cultures is a favorable symptom, while their persistence is unfavorable. Elevation of temperature late in the disease is often accompanied by a return of the organisms to the fluid.

DIAGNOSIS

For a certain diagnosis the bacteriological identification of the meningo-coccus in the cerebrospinal fluid is essential, as is a positive blood culture in the premeningitic stage.

No symptom-complex is pathognomonic of meningococcic infection. An acute onset with fever, vomiting, severe headache and malaise accompanied by cerebral symptoms, especially meningismus, are strongly suggestive of meningococcic meningitis, but the same train of symptoms may usher in such acute infections as typhoid fever, influenza, pneumonia, otitis media and acute malaria. A hemorrhagic rash is strongly suggestive of meningococ-cemia, but it also occurs in the malignant form of measles and in pneumo-coccic and streptococcic infections.

Lumbar puncture is the only positive method of distinguishing the con-dition from other forms, such as the tuberculous and pneumococcic menin-gitis. Certain clinical differences aid in the differentiation but in sporadic cases the spinal fluid furnishes the final evidence. There are cases which, from purely clinical evidence, are unquestionably meningococcic but which fail to reveal the microörganisms in the spinal fluid although it is turbid from the presence of polymorphonuclear leukocytes. These cases should be treated as meningococcic meningitis and recovery is in favor of this diag-nosis as meningitis due to the other organisms is usually fatal. The diagnosis in these cases is more academic than essential as these cases usually respond to the therapeutic test.

In *tuberculous meningitis* the onset is usually insidious, a focus of tuber-culosis is often found elsewhere in the body, herpes is rare, retraction of the head is less marked, opisthotonos is uncommon, and the fluid from the lum-bar puncture is clear, generally shows an excess of mononuclear cells and

often contains tubercle bacilli. *Pneumococcic meningitis* pursues a more rapid and stormy course and is of greater gravity than meningococcic meningitis. When it occurs independently of pneumonia the diagnosis can be made only by finding the pneumococci in the spinal fluid. *Streptococcic meningitis* may be suspected when there is a focus of infection in the middle ear or elsewhere in the body.

The meningitic form of *acute poliomyelitis* has symptoms similar to those of cerebrospinal fever. In this disease, however, the spinal fluid is clear or shows an abundance of mononuclear cells, leukocytosis is less constant than in meningitis and paralysis usuallly appears by the second or third day.

Epidemic encephalitis usually causes milder disturbances of consciousness, rigidity of the neck is slight or absent, ocular paralysis is a conspicuous and early symptom, and the spinal fluid is sterile, clear and shows a moderate increase of small mononuclear cells.

Meningismus, which is a fairly common symptom, especially in children, may be due to a variety of diseases. *Influenza* with its protean manifestations, if accompanied by meningismus, may be differentiated with certainty only by lumbar puncture. Points in favor of cerebrospinal fever are:

    1. Vomiting more frequent

    2. A relatively slow pulse in proportion to the temperature

    3. By the end of the first day Kernig's sign detected

    4. By the second day improvement in the influenzal patient but not in the case of cerebrospinal fever

Pneumonia in children and the apical form in adults is not infrequently ushered in by symptoms of meningeal irritation and should be kept in mind. During an epidemic of cerebrospinal meningitis *tonsillitis* with stiffness of the neck from cervical adenitis has been mistaken for meningitis.

Before the days of lumbar puncture the purpuric eruptions of fulminating and acute cases were often confused with other hemorrhagic conditions, particularly malignant measles.

Infantile convulsions, if followed by a rise of temperature, should lead to a consideration of meningitis. Bulging of the fontanel, present during a convulsion, persists if the case is one of meningitis but disappears if the seizure is due to dietetic or other causes. *Tetany* in infants is not accompanied by neck rigidity and the anterior fontanel does not bulge. *Acute enteritis* in infants is frequently accompanied by convulsions, meningismus is an occasional feature and to add to the difficulty enteritis may occur at the onset of cerebrospinal fever. In an enteric diarrhea the fontanel is depressed rather than bulging. In older children the rapid development of neck rigidity and Kernig's sign elucidate the diagnosis.

COMPLICATIONS

The frequency of complications in cerebrospinal fever has been favorably modified by the therapeutic use of serum. They are more apt to occur in severe cases than in mild ones.

Pericarditis is usually seen only in fatal cases. Temporary cardiac dilatation may occur in the acute type, probably due to the occurrence of cloudy swelling. Endocarditis, phlebitis and embolism are rare complications.

Pneumonia, bronchitis and *bronchopneumonia* sometimes occur. Pneumonia in unconscious patients may be of the hypostatic variety and in such cases changes of position should be insisted upon to forestall congestion and pneumonia. Bronchopneumonia is relatively frequent and is more common in children than in adults. It appears in the more acute cases and is usually fatal. A terminal bronchopneumonia occurs comparatively often. A sudden rise in the respiratory rate is a significant sign, although this takes place also in the coma which precedes death.

The complication of *pyelitis* varies with different epidemics; in some it is rather frequent and in others it is rare. Pyelitis sometimes accounts for the persistence of pyrexia after other clinical signs indicate recovery from the meningitis. The pyelitis does not go on to abscess formation. *Cystitis* sometimes develops and in a few cases meningococci have been found in the urine, but more often it is the result of repeated catheterization in patients who suffer from retention of urine. *Epididymitis* is comparatively rare and its incidence varies with different epidemics.

The Articular System.—Pain in the joints is common at the onset of cerebrospinal fever and in the early stages but it is often disregarded in the face of the more severe symptoms. It may accompany hemorrhagic lesions of the skin and is probably due to meningococcic emboli and hemorrhages into the synovial membranes. The pain may be the precursor of synovitis.

Arthritis or *synovitis* is not uncommon. Modern methods of treatment seem to have decreased its incidence. Meningococcic infection of the joints may occur without meningitis. It is due to the meningococci carried to the joints by the blood stream and may develop in connection with other manifestations of metastasis, as in the case of the initial hemorrhagic rash. It is more often seen in adults than in babies but when it does occur in the latter the hands and feet are especially the point of attack, while in adults the larger joints, the knees, wrists and ankles are the seat of the trouble. There are two types of cases: (*a*) Those occurring during the septicemic stage somewhere about the fourth day. In these several joints are attacked which are usually painful, though but slightly swollen. They show local heat and some redness of the skin, and resemble an acute rheumatism. (*b*) The late cases of arthritis which are usually monarticular, the knee being

most commonly involved, purulent, with much local swelling but comparatively little pain or limitation of motion.

The prognosis in regard to the condition of the joint is good. The early cases clear up rapidly while the suppurative cases may respond to simple aspiration. Ankylosis is rare.

Billington reports a series of thirty-five cases of lumbar spondylitis following cerebrospinal fever. These all had frequent lumbar punctures and pain and stiffness in the lumbar region either in the acute or convalescent stage. He considers this a suggestion of direct infiltration by the lumbar puncture, since if the condition were due to trauma it might be expected also in cases of syphilis which are treated by the intraspinous route.

Symptomatic treatment of the articular complication is usually sufficient. Acetyl-salicylic acid will relieve the pain. Intra-articular injection of serum is often recommended and may be resorted to if the joint does not readily clear up.

Ocular Complications.—These, in comparison to tuberculous meningitis, are rare. *Conjunctivitis* is reported by various observers in from 5 to 20 per cent of cases. If it appears early in the disease it is of little significance but a later conjunctivitis may be the beginning of a panophthalmitis. Conjunctival hemorrhages, if present, are of diagnostic importance since they rarely occur in other forms of meningitis. Corneal ulcers may develop and these may yield meningococci as well as the pus of the conjunctivitis. *Optic neuritis* is infrequent in contrast to its high incidence in tuberculous meningitis. *Nystagmus* may be regarded as pathognomonic of internal hydrocephalus and therefore of grave import. *Strabismus* is usually transient and occurs early in the disease, whereas in tuberculous meningitis it is a late manifestation. Retraction of the upper eyelid is an early sign of the posterior basal type which appears in advance of the other symptoms of hydrocephalus.

The Nervous System.—A variety of nervous complications may be presented, many of them rare or inconstant. Facial paralysis, aphasia, paraplegia, monoplegia and hemiplegia are possibilities. The paraplegias which improve slowly indicate that they are due to pressure of exudate, while the more permanent conditions, either rigid or flaccid, depending upon the site of the lesion, are due to adhesions or pressure. Functional paraplegia, due to hypnotic or autosuggestion, responds to vigorous persuasion. Monoplegias and hemiplegias are rare and may be either organic or functional. Nerve deafness may occur.

Hydrocephalus.—Hydrocephalus must be considered under two types, generalized and internal.

Generalized hydrocephalus is the condition due to the accumulation of cerebrospinal fluid under increased tension throughout the entire subarach-

noid space which is invariably present at the beginning of cerebrospinal fever and is responsible for the headache, vomiting and bulging of the anterior fontanel. The condition is relieved by frequent lumbar puncture and may respond to a single one.

It is possible also for a generalized hydrocephalus to develop later in the course of the disease when the symptoms, headache, lethargy, vomiting, and dilated pupils, are practically identical with those of internal hydrocephalus but less severe in type. This condition differs from internal hydrocephalus in that there is no blocking in the circulation of cerebrospinal fluid, and lumbar puncture yields a quantity of fluid under pressure.

Internal Hydrocephalus.—Under normal conditions the cerebrospinal fluid, secreted by the choroid plexus into the lateral ventricles, goes from there into the fourth ventricle and thence to the subarachnoid space through the median foramen of Magendie and the two lateral foramina of Luschka. An inflammatory process, especially with the production of thick pus, may wholly or partially block these foramina, in which case the cerebrospinal fluid accumulates in the ventricle where the increased pressure tends to cause it to dilate.

Posterior basal meningitis is particularly prone to produce this result both in infants and in older patients. The increase of fluid in the ventricles leads to their dilatation and the flattening of the brain tissue against the walls of the cranium. The increased bulk of the cerebral hemispheres crowds the cerebellum against the medulla and assists in the obliteration of the foramen of Magendie. Usually either the foramen of Magendie or the foramina of Luschka remain patent and the one partially compensates for the other. Even though the natural outlet of cerebrospinal fluid is not blocked the tissue surrounding the ventricles, softened by inflammation and edema, yields readily to the increased pressure.

Internal hydrocephalus usually occurs as a late complication, although it may develop at a comparatively early stage. The onset is frequently insidious, beginning with a headache. The patient then becomes lethargic and loses memory for recent events. Children show no interest in their surroundings and lie for hours with a peculiar vacant look. Death is preceded by coma. The peculiar high-pitched purposeless cry (cri hydrocéphalique) is encountered only in extreme cases.

Persistent vomiting, cerebral in origin, and not related to the taking of food, is frequent. Loss of sphincter control is observed. The progressive wasting in spite of the ingestion of considerable quantities of food is probably trophic in origin.

In infants the anterior fontanel is tense and bulging, the sutures may reopen and then become actually enlarged. In older children Macewen's sign can almost always be elicited. This is a hollow note on percussion over

the inferior frontal or parietal bone when the patient is in an upright position with the head inclined slightly to one side.

Muscular twitchings become more pronounced as the condition advances and in children convulsions frequently occur. General hyperesthesia is frequent. Dilatation of the pupils with sluggish reaction to the light is almost constant. Ocular palsies, lateral nystagmus or exophthalmos may occur. In infants suffering from the anterior basal type, blindness of central origin is encountered.

Pulse and respiration show considerable variation. In most cases death results from respiratory failure.

The spinal fluid obtained upon daily lumbar puncture steadily diminishes in quantity till none can be withdrawn.

The early evaluation of the symptoms of lethargy, severe headache with vomiting, tremulousness and dilated pupils, should lead one to recognize impending hydrocephalus. Prompt and repeated lumbar punctures may avert the calamity. When occlusion of the foramina is complete death is invariable. On the other hand, cases which present all the clinical signs of internal hydrocephalus including "dry taps" sometimes recover.

PROGNOSIS

The prognosis in cerebrospinal meningitis has been markedly improved by the discovery and use of the curative serum. Before antimeningococcic serum was in general use the mortality in epidemics ranged from 20 to 90 per cent. Flexner gives statistics in eighteen epidemics in which the death rate ran from 42.5 to 90 per cent. In epidemics in which some cases have been treated with serum and others by different methods the death rates show a difference of as high as 50 per cent in favor of those treated with serum. In a study of 627 cases by Neal *et al.* in New York City during a non-epidemic period the death rate was nearly 30 per cent. In this group a large number of the children were under one year of age. It seems that in a large group of cases the death rate may be expected to stay at 30 per cent or less. Any higher death rate indicates some preventable ineffectualness either in the serum or its administration.

The early administration of the serum gives the best effect. Each day of delay renders the prognosis more grave. The use of serum shortens the period of active symptoms, makes the appearance of complications less frequent and the sequelæ less severe. It serves to inhibit infection, to neutralize the toxemia and to stop the meningitis before adhesions and blocking occur.

Age.—The prognosis is bad at the two extremes of life; before the age of one year and after the age of forty, the mortality is high.

Remote Prognosis.—In spite of its bad reputation as a crippling disease recent studies show that the patient surviving meningitis is not apt to be permanently maimed. Neal found 18 per cent with sequelæ and some of these not of a serious nature.

Day of Death.—More than half of the fatal terminations occur during the first week.

Cause of Death.—The causes of death in general fall into the following groups :

1. Toxemia, especially in the fulminating cases
2. Sudden respiratory failure, due to cerebral hyperemia rather than to hydrocephalus
3. Local cerebral sepsis, especially in the progressively purulent type
4. Hydrocephalus with increased intracranial pressure
5. Secondary bronchopneumonia

The following table gives the mortality rate per 100,000 population in New York State from 1915 to 1925. It will be observed that there is practically no difference between the death rate in the United States registration area and that in New York State. During the years of the World War there was a noticeable increase in the number of deaths both in the cities and the country districts. The urban rate is over twice that found in rural communities, due no doubt to the more congested population and a greater number of carriers.

TABLE XXXIII.—DEATH RATE FOR CEREBROSPINAL MENINGITIS PER 100,000 POPULATION OF THE UNITED STATES DEATH REGISTRATION AREA OF NEW YORK STATE FROM 1915 TO 1925

Year	United States Registration Area	New York State	New York City	New York State Exclusive of New York City
1915	3.2	2.7	2.3	3.1
1916	3.6	3.0	3.6	2.4
1917	5.5	3.1	3.4	2.7
1918	5.9	4.2	4.8	3.5
1919	3.4	2.9	3.1	2.7
1920	3.0	1.8	2.2	1.4
1921	2.6	2.3	2.6	2.1
1922	1.9	1.7	1.9	1.5
1923	2.1	1.8	1.8	1.7
1924	..	1.9	2.5	1.3
1925	..	2.0	2.3	1.5

The mortality rate according to age shows that the greatest number of deaths occur under two years of age, so that very young children are especially susceptible to this disease.

TABLE XXXIV.—DEATH RATE FOR EPIDEMIC CEREBROSPINAL MENINGITIS PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1924, ACCORDING TO AGE

Age, Years	Number		Rate		Per Cent of All Cases	
	1915	1924	1915	1924	1915	1924
Under 1............	40	39	16.5	16.7	.2	.2
1.................	44	17	23.6	8.0	.8	.6
2.................	15	4	7.6	1.8	.7	.3
3.................	11	2	5.7	.9	.9	.2
4.................	6	7	3.2	3.3	.7	.9
5-9..............	33	23	3.7	2.2	1.2	.9
10-14............	13	7	1.5	.7	.7	.4
15 and over......	66	36	.9	.5	.1	.3
TOTAL ALL AGES ..	228	135	2.3	1.2	.2	.1

There seems to be a slight predilection for males in the mortality from this disease.

TABLE XXXV.—DEATH RATE FOR EPIDEMIC CEREBROSPINAL MENINGITIS PER 100,000 POPULATION IN NEW YORK STATE FROM 1915 TO 1924, ACCORDING TO SEX

Year	Male	Female
1915	1.8	1.4
1916	2.4	1.6
1917	3.0	1.6
1918	3.8	2.4
1919	2.5	1.5
1920	1.5	1.1
1921	2.2	1.2
1922	1.5	1.0
1923	1.2	.8
1924	1.4	1.1

TREATMENT

Prophylaxis.—The prophylaxis of cerebrospinal fever consists of: (1) The isolation of patients suffering from the disease; (2) general hygienic measures with special reference to the prevention of the respiratory diseases; (3) search for and treatment of carriers.

In regard to the individual case the usual precautions of strict isolation obtain. Frequent cultures from the nasopharynx of each person who is in any way a contact should be made to insure that no carriers, either transient or chronic, are being produced. Since the meningococcus succumbs when in contact with mild antiseptics it is helpful for nurses and attendants to use non-irritating nasal and throat sprays. A combination of hydrogen peroxid and a 5 per cent argyrol solution is effective. Convalescent patients should not be discharged until three successive cultures from the nasopharynx are negative.

General hygienic measures are important factors in the armamentarium against cerebrospinal fever. The meningococcus perishes at temperatures lower than 71.6° F. and can resist neither sunshine nor drying. Favorable conditions for its growth are a warm moist atmosphere with people in close enough proximity to permit the spread from throat to throat. Army experience shows that fatigue and overcrowding of troops increase the incidence of infection. Fresh air and sunshine, avoidance of overcrowding and of an overheated moist atmosphere all play a part in the prevention. In dormitories sufficient air space between the beds and cool circulating air are essential. Attacks of influenza, tonsillitis and catarrh increase susceptibility and every effort should be made to check the spread of these diseases. During an epidemic those showing signs of respiratory infections should be isolated and watched.

Carriers are the chief source of infection and should be sought for especially among those who have been in contact with the disease. Cultures should be taken from new recruits in a camp and from children entering an institution. The treatment of transient carriers is of little moment since they become negative spontaneously; fresh air and sunshine will be effective without further measures. In the chronic carriers the frequent application of mild antiseptics to the nasal and pharyngeal mucous membrane is recommended. If there is a deformity of the septum or a similar local condition which prevents the spray from reaching all parts it may be necessary to shrink the mucosa by a preliminary spray of adrenalin (1:1,000). Sprays of hydrogen peroxid, dichloramin-T and of the silver salts are effective. Insufflations of dried antimeningococcic serum have been used. When large numbers of carriers are to be treated, as in military camps, steam chambers are used.

The value of prophylactic vaccines is still under discussion. They are not effective in carriers, but as a prophylactic measure in the general population they have been used with success. A multivalent vaccine used by Sophian and Black afforded a high degree of protection of twelve months' duration.

Specific.—The early subdural injection of antimeningococcic serum is of the utmost importance in the treatment of cerebrospinal fever. Far better is the unnecessary introduction of the curative serum than even the remote chance of delaying treatment for a day, especially as no known harm results from the injection of antimeningococcic serum in cases which are not meningococcic meningitis. One great difficulty in treatment lies in the fact that in the subacute type of cases the physician is not called until the disease is well established and the delay in the administration of the serum adds greatly to the gravity of the prognosis.

When the initial lumbar puncture is performed it is the accepted prac-

tice to have at hand the antimeningococcic serum, and if the spinal fluid shows any departure from its characteristic clearness, or if the symptoms of the patient are such as to make it probable that the patient has cerebrospinal fever, to inject a suitable dose without waiting for the laboratory confirmation of the diagnosis. The serum furnished by laboratories is polyvalent and should be used for the first injection and until the type of organism with which one is dealing is determined. As it is always of academic interest to know the type of the invading organism and may be of practical value in dealing with the case, the organism is typed as early as possible.

Lumbar puncture is performed with strict surgical asepsis and without general anesthesia. Infiltration of the skin with novocain may be advisable but the puncture of the skin with the lumbar puncture needle is hardly more painful than that of the needle for the novocain. The patient is placed on his side with the hips perpendicular to the bed and the back arched in order to separate the spines of the vertebræ. The location of choice is the space between the fourth and fifth lumbar vertebræ, which is the notch that falls on the line connecting the crests of the ilia. This notch may be temporarily marked by pressure of the nail before the skin is sterilized with iodin and alcohol. The needle is inserted forward with the point directed a little toward the patient's head, following the upper edge of the lower spinous process, and with great care to keep it laterally perpendicular. It is inserted slowly for a distance of from ½ to 3 inches, depending upon the size and development of the patient. The puncture of the dura gives the sensation of puncturing parchment and when that sensation of "give" is felt the style of the needle is withdrawn. The flow of fluid shows that the subdural space is reached. The fluid is received in a sterile graduate and is allowed to flow until it issues at the rate of four to five drops per minute. Then sterile tubing ⅛ to ¼ inch in diameter and 15 to 18 inches in length is attached to the needle and a small funnel connected to the tubing. The serum, warmed to body temperature, is allowed to flow into the spinal canal with the least possible pressure. The amount injected is from 5 to 10 c.c. less than the amount withdrawn. In children under five years 20 c.c. is probably the maximum amount advisable to use. When the fluid runs in freely after a dry tap one should be particularly watchful for changes in respiration or pulse. If the breathing becomes embarrassed the introduction of the serum is immediately stopped and some of it is allowed to flow out while the needle is still in place.

When the spinal fluid is too thick to flow through the needle, gentle suction by a syringe may start the flow.

In cases of moderate severity the injection of serum should be repeated daily for the first four days or until there is a decided remission of symptoms. The course of the infection may be readily judged by the daily micro-

scopic examination of smears made at the time of lumbar puncture. With improvement the organisms and pus-cells gradually disappear. In very severe cases the serum may be administered every twelve hours.

The repeated spinal drainage is of itself of great therapeutic importance and should be continued after the injections of the serum have stopped. They should be continued until the pyrexia is ended and the spinal fluid is clear microscopically.

While the polyvalent sera from the different laboratories are all standard, there is a difference in the response of different patients to a particular serum. In case the response is disappointing it is advisable to secure the serum for the type of organism in the particular case, or else to use the polyvalent serum from another laboratory.

The *site of lumbar puncture,* as mentioned above, is preferably between the fourth and fifth lumbar vertebræ, but with repeated lumbar punctures it is necessary to vary the location from day to day, otherwise adhesions will form and shut off the subdural space. Puncture above the fourth interspace is theoretically less desirable but it may be performed without harm as high as the twelfth thoracic. Above the eleventh thoracic vertebra it is useless as the arachnoid space is not present.

The *effect* of the first lumbar puncture is a considerable lowering of temperature to normal or below within eight hours, followed by a rise. The fall is due to the evacuation of the purulent exudate and occurs independently of the introduction of serum.

Accidents during the serum injection are infrequent. Embarrassment of breathing is the most common. If this occurs the funnel should be lowered and the serum which has entered the subarachnoid space allowed to escape through the lumbar puncture needle. If breathing stops the administration of atropin in full doses and artificial respiration will restore the function.

The Intravenous Injection of Serum.—As has been pointed out, the first stage of cerebrospinal meningitis is a general septicemia. Whenever the diagnosis of this premeningitic stage can be made, as is the case during epidemics, the proper treatment is the intravenous injection of the anti-meningococcic serum. Herrick has found this treatment safe and satisfactory. Large quantities of serum (200-600 c.c.) are given. One intravenous injection is probably all that is justified and while it is essentially dangerous the method should be employed only when the diagnosis of severe infection in the premeningitic stage is made.

General Management of Symptoms.—The sick room should be quiet, darkened and supplied with an abundance of fresh air. The diet should be an abundant one of easily digested food. The appetite is usually well maintained and the digestive system not greatly disturbed. Nursing babies

should be kept on breast milk. Older children should be on a liquid diet at first, but semisolid food in such form as custards and cereals may be begun before the pyrexia has subsided. If stupor is present tube feeding of milk, plain or peptonized, will maintain the nourishment.

Constipation is usually present and is treated with cathartics and enemata. One must watch for retention of urine and catheterize when necessary.

For the pain and restlessness an ice-cap to the head is comforting. Many patients are soothed by hot baths (temperature 104° F.), in which case they may be given twice a day. In mild cases the bromids, acetyl-salicylic acid or allonal will control the pain, but in the more severe cases it is necessary to give morphin hypodermically.

If a cardiac stimulant is indicated, digitalis should be given, as caffein and strychnin tend to increase nervous excitability.

Various drugs have been advocated from time to time in the treatment of cerebrospinal meningitis but have been tried and found wanting and discarded one by one. The most prominent of these has been hexamin but the clinical results have been disappointing.

Aside from the serum the treatment is symptomatic and the clinician must be guided by the daily condition of the patient.

Complications.—The two most grave complications are bronchopneumonia and hydrocephalus and treatment should be directed toward their prevention. *Bronchopneumonia* can best be avoided by the nursing care of the patient. It is quite likely to arise as a hypostatic condition and frequent changes in the position of the patient will prevent congestion in any particular area of the lungs.

When there is evidence of *increased intraventricular pressure* which is not relieved by spinal drainage, drainage of the ventricles is indicated. In infants this is easily accomplished by the introduction of the needle into the ventricle through the lateral angle of the anterior fontanel, but in older patients preliminary trephining is necessary. If the aspirated fluid is purulent a small amount of serum may be introduced, following the aspiration.

Puncture of the cisterna magna sometimes proves to be a more effective way of relieving pressure than either ventricular or lumbar puncture. This procedure, while potentially dangerous, has been accomplished successfully many times (Peet) and the hazard may well be incurred rather than that of increasing hydrocephalus.

The *arthropathies* usually respond to immobilization and warm applications. A large amount of fluid in a joint may call for aspiration, following which the injection of a small amount of the antimeningococcic serum usually results in a prompt subsidence of symptoms.

Pyelitis and *cystitis* are treated by hexamin or potassium citrate in appropriate doses.

A *flaccid paralysis* calls for the protection of the joint with appropriate appliances to prevent stretching of the weakened muscles. Massage and passive movements should be instituted early in convalescence to restore these muscles.

Deafness of central origin does not yield to treatment. Potassium iodid is often given but without definite results.

SERUM DISEASE

Serum disease results from the introduction into the circulation of a protein foreign to the organism. Probably it does not occur more frequently from subdural injections of serum than from intravenous, but owing to the repeated use of the serum in cerebrospinal fever it is essential that the condition be promptly recognized.

Symptoms.—The commonest manifestation of serum disease is the appearance of a rash, usually from eight to ten days after the administration of the first dose of serum. It may occur from the fifth to the sixteenth day. It is urticarial or erythematous in character, rarely petechial or purpuric. It may last only a few hours but the usual duration is two days. Occasionally two separate rashes with a free interval are observed.

Arthralgia is often complained of. Adenitis, cervical and inguinal, transient albuminuria, and diarrhea may be present. When pyrexia occurs it usually follows the disappearance of the rash and lasts from two to four days. In severe cases edema of the tongue, uvula, scrotum and penis may occur.

In a few cases serum disease may appear in the form of meningeal irritation, in which case it must be carefully distinguished from an exacerbation of the meningitis since the injection of a large quantity of serum would gravely aggravate the condition. If the meningitis has cleared up, the lumbar puncture will yield a clear fluid containing comparatively few cells, meningococci will be absent and glucose, which is absent during the meningitis, will be present. Furthermore, with the recrudescence of the meningitis the white blood-cell count is increased, but not with serum disease.

Treatment.—For the mild form of serum disease no treatment is necessary further than bathing with a warm solution of bicarbonate of soda to relieve the itching of the rash. A hypodermic injection of adrenalin chlorid, 5 to 10 minims, will promptly relieve the urticaria. For severe edema hypodermic injections of pituitrin are effective.

Anaphylaxis, of which serum disease is a manifestation, must be particularly guarded against if it becomes necessary to resume the injection of

the serum after an interval of ten days. It is then essential to desensitize the patient (see diphtheria for technic) before the administration of the serum.

SEQUELÆ

The sequelæ which follow cerebrospinal fever arise for the most part during the acute stage of the disease and are directly due to the inflammatory process. Neal found 18 per cent of cases and McLean and Caffey found 20 per cent with sequelæ.

Deafness is the most frequent. It is usually bilateral, complete and permanent and if it occurs in young children is often accompanied by mutism. It is a nerve deafness.

Mental deficiency may be the result of hydrocephalus, but mental impairment is not so general as has been popularly believed. In Neal's cases 2 per cent showed some mental disturbances. In adults psychical changes, such as irritability, loss of power of attention or memory and of ability to concentrate, are reported.

Blindness, due to optic atrophy, may occur in infants who have had the posterior basal type of the disease.

Pain in the back with weakness and stiffness is almost always complained of during convalescence. That this is not due to the mere fact of repeated lumbar puncture is borne out by the fact that this procedure in cerebrospinal syphilis does not produce a similar result.

Paralysis of the limbs may persist for several months after recovery, but in most cases the full power is eventually restored. Weakness of the legs and unsteadiness of gait are frequent during convalescence.

PUBLIC HEALTH REGULATIONS

The New York State Department of Health requires that a physician attending a case of epidemic cerebrospinal meningitis shall report it within twenty-four hours to the local health officer, stating the name, age and address of the patient. All such cases are quarantined for a period of not less than two weeks after the temperature has become normal or until three successive cultures, obtained from the nasopharynx at intervals of not less than five days, have been examined in a laboratory approved for this purpose by the State Commissioner of Health and found free of meningococci.

Carriers detected by bacteriological methods are quarantined until the nasopharynx is free from meningococci.

If there are other children in the same household and the patient is quarantined in the home, they are excluded from school and social gatherings for one week after the termination of the quarantine. If the patient

goes to a hospital or if the other children leave home when the disease is discovered, they are not allowed to attend school until one week from the date of removal.

The present knowledge of cerebrospinal meningitis as summarized by the American Public Health Association is as follows:

1. INFECTIOUS AGENT.—Meningococcus; *Neisseria intracellularis.*

2. SOURCE OF INFECTION.—Discharges from the nose and mouth of infected persons. Clinically recovered cases, and healthy persons who have never had the disease but have been in contact with cases of the disease or other carriers, act as carriers and are commonly found, especially during epidemics. Such healthy carriers are not uncommonly found independent of epidemic prevalence of the disease.

3. MODE OF TRANSMISSION.—By direct contact with infected persons and carriers, and indirectly by contact with articles freshly soiled with the nasal and mouth discharges of such persons.

4. INCUBATION PERIOD.—Two to ten days, commonly seven. Occasionally for longer periods when a person is a carrier for a time before developing the disease.

5. PERIOD OF COMMUNICABILITY.—During the clinical course of the disease and until the specific organism is no longer present in the nasal and mouth discharges of the patient. The same applies to healthy carriers so far as affects persistence of infectious discharges.

6. METHODS OF CONTROL

    (*a*) The infected individual and his environment

        1. *Recognition of the Disease.*—Clinical symptoms, confirmed by the microscopic and bacteriological examination of the spinal fluid, and by bacteriological examination of nasal and pharyngeal secretions.

        2. *Isolation* of infected persons until fourteen days after onset of the disease.

        3. *Immunization* by the use of vaccines is still in the experimental stage.

        4. *Quarantine.*—None.

        5. *Concurrent disinfection* of discharges from the nose and mouth and of articles soiled therewith.

        6. *Terminal disinfection.*—Cleaning.

    (*b*) General measures

        1. Search for carriers among families and associates of recognized cases by bacteriological examination of posterior nares of all contacts.

        2. Education as to personal cleanliness and necessity of avoiding contact and droplet infection.

        3. Prevention of overcrowding such as is common in living quarters, transportation conveyances, working places, and places of public assembly in the civilian population, and in inadequately ventilated closed quarters in barracks, camps, and ships among military units.

(*c*) Epidemic measures

1. Increase the separation of individuals and the ventilation in living and sleeping quarters for such groups of people as are especially exposed to infection because of their occupation or some necessity of living conditions. Bodily fatigue and strain should be minimized for those especially exposed to infection.

2. Carriers should be quarantined until the nasal and pharyngeal secretions are proved by bacteriological examination to be free from the infecting organism.

CHAPTER XVI

TETANUS

Tetanus is an acute disease of infectious origin, characterized by painful spasms of the muscles and caused by the toxin of the *Bacillus tetani* elaborated at the site of inoculation which is always some wound or break in the skin.

History.—Lockjaw or tetanus has been recognized as a clinical entity for many centuries but the infectious nature of the disease was not demonstrated until 1884 when Carlo and Rattone produced tetanus in rabbits by the inoculation of pus from the cutaneous lesion of a human case. Nicolaier the next year produced tetanic symptoms in mice and rabbits by inoculating them with soil. Nicolaier was not able to cultivate his organism in pure culture but Kitasato (1889) established the bacillus as the causative factor by obtaining pure cultures from cases of tetanus by which he reproduced the disease in animals. Kitasato was successful because he grew his organisms under anaërobic conditions and eliminated the non-spore-bearing organisms by means of heat.

BACTERIOLOGY

Occurrence.—The normal habitat of the tetanus bacilli is the intestine of the herbivora. They are present in about 15 per cent of the horses and calves in the vicinity of New York City and in the feces of other domestic animals and man. Some animals offer especially favorable conditions for the growth of the bacilli and these are known as tetanus carriers. The bacilli are found both in the superficial and deep layers of the soil, and cultivated and manured fields show its presence with greatest frequency, probably carried there by the dejecta of the domestic animals. The spores may be found in soils, street dust, on fresh vegetables and on clothing and the skin. There appears to be a regional distribution and in the United States it appears most frequently in the Hudson Valley, in the Atlantic states on Long Island, and in California.

Human Carriers.—Recent work indicates that man is a tetanus carrier in a much larger proportion of cases than had formerly been supposed. Ten Broeck and Bauer in 539 specimens of human feces from various parts of China found the organism in 153 instances or 26 per cent. Bauer and

Meyer examined 487 specimens in California and found tetanus spores in 24.6 per cent of the cases. These were all toxic strains. Tulloch isolated tetanus bacilli in 16 per cent of cases in a study made in England. It appears therefore that the bacilli are widely distributed and that carriers have a wide geographical distribution.

Morphology and Staining.—The bacillus of tetanus is an anaërobic, liquefying, moderately motile bacillus. In young cultures it has abundant, peritrichal flagella in the vegetative form which are lost in the spore-bearing stage. It is a slender rod 2 to 4 micra in length and 0.3 to 0.5 micron in diameter. The vegetative forms show a wide variation from short rods to long filaments which later break up into bacilli. They form spherical spores, thicker than the cell, located at one end which makes them appear like drumsticks or small pins. The bacillus is stained with the ordinary aniline dyes and is not decolorized by the Gram method.

Cultural Characteristics.—The bacillus of tetanus is naturally an anaërobe, but anaërobic conditions may be dispensed with if it grows in symbiosis with aërobic bacteria. The addition to the culture-media of suitable carbohydrates or of fresh sterile liver tissue has been found to favor growth under conditions not strictly anaërobic.

Colonies of *B. tetani* have a tendency to grow as a spreading film upon the surface of the medium. If the water of condensation of a sloped agar tube is inoculated with the bacillus, the growth in two days will spread to the apex of the surface. If the strain is not pure the contaminating organisms will not spread to an equal height and reinoculation will result in a pure culture.

It grows most luxuriously on *peptic blood agar* but also successfully upon ordinary agar. The growth spreads as a film upon the surface which has the macroscopic appearance of dew upon glass, and later of ground glass. Microscopically the film is made up of long spreading filaments. Upon the sloped tube the stationary upper edge, after seventeen to twenty-four hours, shows fine threads of the bacilli reaching upward, nearly horizontally.

On gelatin plates the colonies develop slowly and have a dense opaque center surrounded by fine diverging rays.

Gas is produced in most media which has a characteristic and very disagreeable odor.

Resistance of the Spores.—The vegetative forms of the tetanus bacillus are destroyed by heat and chemical agents in about the same degree as other microörganisms, but the spores exhibit remarkable resistance to deleterious influences. In a desiccated condition and protected from sunlight the spores remain viable and virulent for many years, but direct sunlight eventually destroys them. The spores will resist dry heat at 80° C. for one hour, but are destroyed by an exposure of ten minutes to live steam

at 105° C. Five per cent carbolic acid kills them in twelve to fifteen hours; 1 per cent of bichlorid of mercury in two to three hours. Silver nitrate solutions destroy the spores of average resistance in one minute in 1:100 solution and in five minutes in 1:1,000 solution. Putrefying material is favorable to their preservation and they may remain quiescent in wounds from one to three months and then grow and elaborate their toxins when a favorable opportunity occurs.

Types of Bacilli.—At least seven strains of bacilli which are morphologically and culturally true tetanus bacilli have been isolated by agglutination. It has been found, however, that the toxin and antitoxin are not specific, but that antitoxin prepared from any one type will neutralize the toxins of all types. While formerly it was customary to prepare antitoxin by the injection into the horse of the toxin of Type I the toxins of several strains are now used.

Pathogenicity.—In comparison to the wide distribution of the tetanus bacillus in nature the occurrence of tetanus is of comparatively rare occurrence. The spores introduced into the body are overwhelmed by phagocytosis and other protective mechanisms of the body and produce toxin before the vegetative forms develop. The presence of other microörganisms, particularly the common pus cocci, in combination with some tissue destruction and foreign material as dirt, or wood splinters, form an environment suitable for the growth of tetanus bacilli. Taken into the gastro-intestinal tract they are harmless.

Animals vary greatly in their susceptibility; fowls are scarcely susceptible at all, horses frequently develop tetanus after operations or injuries. Mice and guinea-pigs are very susceptible. Animals inoculated with a pure culture develop tetanus in from one to four days.

Tetanus Toxin.—The pathogenicity of the tetanus bacillus depends upon the soluble toxin that it produces. Anaërobic conditions are most favorable to its development. The toxin can be separated from the bacteria by filtration through a Berkefeld filter. In solution it deteriorates rapidly and is extremely sensitive to heat.

Tetanus toxin is one of the most powerful poisons known. Its harmful action is due to its affinity for the central nervous system. It is believed that the toxin is conducted to the nerve-centers along the paths of the motor nerves, probably by way of the lymphatics of the nerves rather than by the axis cylinder. The toxin ascends along the motor path, reaches the spinal ganglia on the side of the inoculation, then spreads to the ganglia of the opposite side and makes them hypersensitive. The increased muscle tonus results in rigidity. In the further course of the poisoning the toxin affects the nearest sensory apparatus with an increase in the reflexes. As it ascends it affects more and more of the motor centers and the neighboring sensory

apparatus. This leads to spasm of the striated muscles and general reflex tetanus. If the toxin gets into the blood the only pathway of absorption is by the motor pathways. The toxin enters into a loose union with the gray matter of the spinal cord and brain.

PATHOLOGY

Few and insignificant lesions are revealed by autopsies upon human beings or animals dead from tetanus. The initial point of infection may be small and insignificant or may show some pus, which in addition to the usual organisms may show some tetanus bacilli or their spores. The organs show a general and moderate congestion. The lesions in the central nervous system are obscure. Congestion, cellular exudate into the perivascular spaces and chromatolysis of the ganglion-cells are common. The bacilli may be cultivated from the spleen and heart's blood. It has also been shown that the spores may be transported from the site of inoculation to the liver, spleen and other organs and lie dormant for six to seven weeks. If the organ is experimentally injured the spores may develop and tetanus follow. Spores or bacilli may lie dormant at the point of infection until activated by some injury or operation. This is the explanation of the delayed or cryptogenic cases of tetanus.

Period of Incubation.—Usually from five to fifteen days elapse between the reception of the wound and the occurrence of symptoms. This is the time required for the bacilli to multiply and elaborate toxins to a degree sufficient to produce symptoms. Toxin is probably produced after the first twenty-four hours following infection and absorption may begin at once. Symptoms may be delayed as long as four months, a condition rather common since the extended prophylactic use of the antitetanic serum. It may occur after the complete healing of the wound, in which case it is usually in connection with some secondary activity at the site of the wound. In general the more severe the infection, the shorter is the incubation period.

SYMPTOMS

Prodromal Symptoms.—The premonitory symptoms are varied and changeable. General restlessness alternating with a desire to rest, sleeplessness, irritability and unreasonable outbursts of temper, distressing dreams or delirium may be noted. Transitory difficulty in micturition, temporary giddiness, violent headache and excessive yawning have been observed. The patient looks anxious, the tongue trembles and when extended is drawn to one side. There may be profuse sweating and darting pains. The muscles may be in a state of increased irritability, the muscles on the side of the

wound may be more rigid than those of the uninjured side and there may be some swelling and throbbing of the arteries.

Characteristic Symptoms.—Following a feeling of soreness and stiffness in the back of the neck and about the jaws there follows a tonic spasm of the muscles of mastication which results in the inability to open the mouth (lockjaw or trismus). By degrees the spasmodic contraction extends to other muscles, particularly the back, face and abdomen, until in time nearly every muscle of the body is affected, with the exception of those of the forearm and hand. Less commonly the contractions begin in the muscles of the wounded part, gradually ascend and become general. When the disease is at its height the characteristic facies develops, the brows are contracted in an expression of distress, the angles of the mouth drawn up as in laughing (risus sardonicus), the eyes partially closed, teeth tightly clinched, and lips slightly protruding. The muscles of the abdomen are rigid, then the back becomes straight and rigid, or more commonly arched, so that only the occiput and heels touch the bed. This *opisthotonos* is a most pronounced and troublesome symptom. Occasionally the body is bent to one side or forward. At intervals, following even a slight stimulation, there occur cramplike paroxysms attended by severe pain and perhaps by profuse perspiration. These clonic seizures may be so severe as to almost hurl the patient from the bed.

The temperature is variable. Mild attacks may be afebrile, but the temperature may rise to 103° or 104° F., especially during the paroxysms, and just before death it may rise to extreme heights. Dragging pain in the chest, dyspnea and cyanosis are frequently met. A coated tongue and an obstinate constipation are the rule. Incontinence or retention of urine may occur. The mind remains clear and the suffering is intense. Death may occur in less than twenty-four hours, but the disease may continue for a week or more. Death may be due to exhaustion, to heart-failure or to asphyxia due to spasm of the laryngeal or respiratory muscles.

A favorable outcome is indicated by a gradual diminution of the number of spasms and a lessening of their intensity. After the lapse of a week every day renders the prognosis more favorable.

Delayed Tetanus.—Tetanus which develops in persons who have received prophylactic injections of antitoxin frequently does not show the characteristic symptoms and is delayed in its appearance. Trismus and general symptoms may not be observed. Manifestations of the disease are frequently confined to spastic rigidity in the wounded limb which may persist for months and then disappear or may develop into general tetanus. Local tetanus should always be suspected when there is a history of injury, when antitoxin has been given, and when pain or stiffness is experienced in the neighborhood of the wound. Localized tetanus should be regarded as

serious, as it may become generalized, even after the wound is healed. Restriction of the lateral movement of the mandible is a symptom of oncoming generalized tetanus.

Tetanus neonatorum.—Tetanus neonatorum is caused by infection of the umbilical wound and is still prevalent in hot climates, arising from the poor sanitation of the ignorant and illiterate. The symptoms come on in a few days or may be delayed for ten days. Trismus and difficulty in crying and in taking food are the first symptoms, followed by general spasms. Mortality is extremely high.

DIAGNOSIS

The spasms of *strychnin poisoning* resemble those of tetanus poisoning but they come on more suddenly, usually attack the muscles of the extremities, affect the jaw muscles very late, if at all, are separated by periods of complete relaxation and quickly terminate in death or recovery.

Tetany shows an absence of trismus, the peculiar flexion of the hand (accoucheur's hand), the commencement of the spasms in the extremities, the different etiological factors.

In *hydrophobia* and *cerebrospinal meningitis* the history should establish the differentiation.

Hysterical convulsions occur chiefly in the neurotic, there is no history of a wound, consciousness is usually affected, emotional disturbances are common and the spasms often begin suddenly.

Tonsillitis and *pharyngitis* may give rise to a condition suggesting trismus, but opisthotonos and rigidity of the neck are absent and there is no history of injury.

Recognition of localized tetanus may be difficult unless a careful history is taken. Any increase of muscle tone, local or general, should be regarded with suspicion when there is a history of a previous injury by which infection might have occurred.

INCIDENCE

In untreated wounds the probability of developing tetanus depends upon several factors: (1) The character of the wound, (2) the amount of contamination, (3) the bacterial flora of the soil with which the wound is contaminated, and (4) the location of the wound.

Clean wounds are not usually followed by tetanus, but deep suppurating wounds which harbor dead tissue and are soil-contaminated carry a grave possibility of the development of the disease. Wounds that are granulating are usually not infected. Wounds of the leg appear more likely to be infected than those of other parts.

The tenth day after a wound is the one upon which symptoms commonly develop and after the third week the risk is very slight.

In America the most prolific source of tetanus has been the wounds following the powder burns of Independence Day, contaminated by street dirt or garden soil. In Flanders the heavily manured soil ground into the crushing wounds of shrapnel gave rise to an appalling number of cases of tetanus before the prophylactic use of serum was made a routine measure. Wolfe found that before December, 1914, without antitoxin 1.4 per cent of the wounded developed tetanus; in the seven months following that date all grenade and shrapnel wounds received antitoxin, with an incidence of 0.16 per cent.

The wounds received in civilian life, if freed from contamination and crushed tissue and treated with a prophylactic dose of 500 units of tetanus antitoxin, have an extremely good chance of escaping infection.

In 1925 the mortality from tetanus in New York State was 0.54 per 100,000 population.

PROGNOSIS

Several factors influence the prognosis. *Age* and *sex* are not of importance.

Incubation Period.—The incubation period is important. In general the more delayed the onset of symptoms the better the prognosis. In Sir David Bruce's first series of 231 cases, with an incubation period of ten days or less, 66.6 per cent died; incubation period of eleven to twenty-five days, 39 per cent died.

Where there is no history of a wound the majority of cases recover.

Survival Period.—Modern experience confirms the observation of Hippocrates that if the patient survives the fifth day the chances are slightly in favor of recovery. After the tenth day the probability of recovery is good.

Severity of Symptoms.—The occurrence of frequent and powerful spasms which indicate the involvement of the cerebrum as well as the cerebellum and the spinal cord renders the prognosis practically hopeless.

High fever is a serious indication.

When *trismus* is the earliest symptom the prognosis is less favorable than when it occurs as a late symptom.

Patients who develop tetanus after a prophylactic injection of antitetanic serum do better than those who have not been so treated.

Local tetanus in which spasm and rigidity are confined to the wounded limb may last for months but is seldom fatal.

In cases that recover, the spasms, if they occur at all, are few and slight.

TREATMENT

Prophylaxis.—The ideal breeding place for the tetanus bacillus is found in the dead putrefying tissues of earth-contaminated wounds such as are caused by dirty pieces of shell or Independence Day burns and wounds. The heavily manured soil of France teems with the bacilli which found easy entrance to the war wounds and produced an appalling number of cases of tetanus during the first months of the World War before the routine use of prophylactic serum and wide excision of the wounds became the routine procedure. It is evident that when nations can settle their differences without recourse to war and Americans can express their patriotism without firecrackers and toy pistols the two great sources of tetanus will be eliminated.

The immediate treatment of penetrating wounds by removal of all crushed tissue, the application of an antiseptic and the administration of antitetanic serum will take care of a large percentage of the potential cases.

In civilian life probably 1 per cent of puncture wounds most liable to infection receive treatment by a physician. One must therefore impress upon the lay public the necessity of precautions in the treatment of minor penetrating wounds, especially those contaminated by street dirt and garden soil and those caused by rusty nails. Even the most innocent looking wound should be treated with an antiseptic, tincture of iodin, or preferably mercurochrome which is not painful, and should be bandaged lightly to keep out dirt and admit the entrance of air. They should be taught to bring the crushed and contaminated wounds to their physician for prophylactic antitoxin injection.

Prophylactic antitoxin is most effective when administered within twenty-four hours after the wound has occurred. The dosage has been given variously from the 500 units advocated by the British War Commission to 1,500 favored by American practitioners. An adult dose of 1,000 units is conservative and effective. Based upon this dosage one may estimate a dose for a child at 40 units per pound of body weight. The dose should be repeated within seven to ten days. The serum is given subcutaneously and is given as near the wound or the main nerve trunk leading from the wound as is practicable.

The wound should be thoroughly cleansed, all foreign material scrupulously searched for and removed, crushed tissues removed, sinuses and recesses opened up and free access of air allowed.

General Treatment.—The aim of the symptomatic treatment is the conservation of strength until the natural defenses of the patient can overcome the effects of the toxin. In the highly sensitized condition of the nervous system the patient responds to slight stimulation with explosive convulsions which are painful and exhausting. The requirements are a quiet,

darkened, well-ventilated room with but one person in attendance who is quiet, tactful and acceptable to the child. Any attention or procedure which is disturbing results in more harm than good. Rattling windows, a squeaking bed and noisy footsteps are to be avoided.

An easily digested and nourishing diet is required. When trismus is present either nasal or rectal feeding will be called into play. Nasal feeding is usually no more irritating than rectal feeding and is more certain of assimilation. A few breaths of chloroform may be necessary before passing the nasal catheter. Milk will provide the protein requirements of a child under five years of age, the caloric value of which may be increased by the addition of lactose, dextrimaltose, or cane sugar and cream. Egg yolks may be added to the feeding but the burden of metabolism of the egg albumin is better avoided in the young patient. Children over five may be given milk, one or two eggs daily, the sugars and cream.

Salines, castor oil and enemata may be used to keep the gastro-intestinal tract clear. Milk of magnesia is harmless and often effective.

The patient should be watched carefully for retention of urine which is a frequent and early symptom. When this occurs catheterization every eight hours is necessary.

Warm baths once or twice during the day will be found beneficial and comforting. Beginning at body temperature they may gradually be raised to 101° F.

Dehydration of the tissues should be combated by the use of proctoclysis.

Antitoxin.—The four avenues of administration of tetanus antitoxin are the intraspinous, the intravenous, the intramuscular and the subcutaneous. By the *intraspinous* method the antitoxin comes in contact with the toxin that has already reached the central nervous system and the purpose is to neutralize the toxin before it becomes bound up in the nerve-cells. The amount of serum that can be introduced into the spinal canal cannot exceed the amount of spinal fluid that can be withdrawn. In adults this is usually not more than 20 c.c. A high potency serum is essential in order to secure an adequate dose of antitoxin. One that carries 800 units to the cubic centimeter allows the introduction of 16,000 units in 20 c.c. of serum. The injection of serum must be made very slowly. The lumbar puncture can best be made under general anesthesia. The introduction of the serum into the subarachnoid space often produces turbidity of the spinal fluid, due to a leukocytosis, with an accompanying meningeal irritation. These symptoms quickly pass off and need not be a cause for alarm.

The *intravenous* injection is given to neutralize the toxin in the blood stream and usually is not repeated after the first day. The usual precautions against anaphylactic shock should be employed, and the serum suitably diluted with a physiological salt solution.

The antitoxin given *intramuscularly* is absorbed in about twelve hours. It is given as near to the site of the wound as is practicable and its function is to neutralize the toxin already in the blood and to prevent absorption by the nerve-endings.

The *subcutaneous injections* are absorbed in about forty-eight hours and are useful in keeping up the antitoxic properties of the blood.

The following table of dosage is recommended by the New York City Department of Health:

Day	Intraspinally	Intravenously	Subcutaneously
First	5,000 to 10,000	10,000	
Second	5,000 to 10,000		
Third	5,000		
Fourth			5,000 to 10,000

If one computes the adult dose of 10,000 units as equivalent to 70 units per pound of body weight, the following table is the corresponding dosage for a child of 50 pounds:

Day	Intraspinally	Intravenously	Subcutaneously
First	3,500	3,500	
Second	3,500		
Third	2,000		
Fourth			3,500

In any case of doubt it is well to give the maximum dosage.

The British War Office Committee on the Study of Tetanus recommends intraspinous and intramuscular injections, but not intravenous injections.

Nicoll, who, with Park, was an early advocate of the intraspinal route of administration of the antitoxin in a recent analysis of statistics, finds that this method does not show marked superiority in its results over the intravenous method alone or in combination. However, animal experimentation and clinical experience are both in favor of the intraspinal route.

As soon as tetanus is diagnosed or suspected no time should be lost in the administration of the antitoxin; each hour of delay renders the prognosis more grave. If only a small amount of antitoxin is at hand it is best to give it as nearly as possible the full intraspinal dose.

In purely localized tetanus small doses in the neighborhood of 5,000 units may be given intramuscularly every second or third day, but with the first symptoms of generalized tetanus the full intrathecal dose should be given without delay.

Surgical.—The wound which has been the port of entry of the tetanus bacillus should be opened widely and mechanically cleansed of sloughs,

crushed tissue and foreign bodies, then swabbed out with a 3 per cent solution of iodin, rinsed with hydrogen peroxid and filled loosely with gauze soaked in iodin. Caustics should be avoided, as the formation of sloughs and eschars provides conditions favorable to anaërobic growth.

Drugs.—The purpose of drugs in the treatment of tetanus is to control the overactivity of the spinal reflexes. Dosage must be sufficient to produce this effect but should be decreased as soon as possible as there is a tendency for the drugs to accumulate in the gastro-intestinal tract and then be absorbed in overwhelming amounts when a change for the better occurs. By means of the antitoxin one aims to stop the formation of new toxin and also neutralize the free toxin, but the occurrence of nervous symptoms is evidence that a large amount of the toxin is already bound up in the central nervous system, particularly the spinal cord. Until its action is exhausted it will continue to stimulate the motor and to a less degree the sensory tracts of the cord. In an uninterrupted course of tetanus, the patient dies from exhaustion.

The sedative drugs are the most useful ones. Chloral and the bromids have proved efficient. The bromids are not cardiac depressants and may be given without fear of cumulative effects. A two-year-old child may take 7 to 10 grains of *potassium bromid,* well diluted, every two hours. *Chloral,* although a cardiac depressant, is useful. For the two-year-old child, 2 or 3 grains every hour will prove an efficient sedative. *Luminal* (phenobarbital) has recently been advocated. The adult dose is 3 to 5 grains by mouth or by rectum. *Chloretone* according to Hutchings will control the muscular manifestations and no fatal cases have been reported following its use. The adult dose is from 30 to 60 grains dissolved in weak alcohol if given by mouth, or in hot olive oil if by rectum.

The use of magnesium sulphate to control the spasm has been the subject of much discussion. The British War Commission decided against its use, and there is a general agreement that its effects must be watched carefully. In those cases where it is impossible to obtain antitoxin promptly it may be tried. The dose is one cubic centimeter of a 25 per cent solution of magnesium sulphate for every twenty-five pounds of body weight, to be given intraspinously.

The injection of *carbolic acid* has fallen into disuse.

The spasms are controlled by the inhalation of *chloroform.*

Morphin sulphate in appropriate doses should be used when necessary to keep the patient quiet.

Tetanus is included among the communicable diseases by the Sanitary Code of the New York State Department of Health and as such must be reported within twenty-four hours to the local health officer. No isolation or quarantine is required.

PUBLIC HEALTH REGULATIONS

The report of the Committee on Standard Regulations of the American Public Health Association summarizes tetanus as follows:

1. INFECTIOUS AGENT.—Tetanus bacillus; *Clostridium tetani.*

2. SOURCE OF INFECTION.—Animal manure, soil, and street dust.

3. MODE OF TRANSMISSION.—Inoculation, or wound infection.

4. INCUBATION PERIOD.—Four days to three weeks, or longer, if latent bacilli deposited in the tissues are stirred to activity by subsequent chemical or mechanical irritation. Commonly eight to ten days.

5. PERIOD OF COMMUNICABILITY.—Patient not infectious except in rare instances where wound discharges are infectious.

6. METHODS OF CONTROL

   (*a*) The infected individual and his environment

   1. *Recognition of the Disease.*—Clinical symptoms; may be confirmed bacteriologically.

   2. *Isolation.*—None.

   3. *Immunization.*—By at least one, and preferably two, injections of antitoxin.

   4. *Quarantine.*—None.

   5. *Concurrent Disinfection.*—None.

   6. *Terminal Disinfection.*—None.

   (*b*) General measures

   1. Supervision of the practice of obstetrics.

   2. Educational propaganda such as "safety-first" campaign, and "safe and sane Fourth of July" campaign.

   3. Prophylactic use of tetanus antitoxin where wounds have been acquired in regions where the soil is known to be heavily contaminated, and in all cases where wounds are ragged or penetrating.

   4. Removal of all foreign matter as early as possible from all wounds.

   5. Supervision of biological products, especially vaccines and sera.

CHAPTER XVII

SEPTIC SORE-THROAT

Definition.—An acute infection of the tonsils and throat caused by the streptococcus group of bacteria and characterized by extreme swelling and soreness of the throat, enlargement of the cervical lymph glands and marked prostration. It is communicable, often appears in epidemic form, and is frequently spread through milk.

Synonyms.—Streptococcus angina, epidemic sore-throat, streptococcic sore-throat, glandular fever.

History.—The relationship between an explosive epidemic of acute sore-throat in sharply localized areas and the milk supply of such areas has been recognized in England for many years. Savage has abstracted reports of eighteen such epidemics which occurred in England between 1880 and 1904 and one which appeared in Christiania which involved 548 reported cases and probably many unreported ones. In all of these there is reasonable evidence to suppose that the infection was spread by the milk supply, although the means by which the milk became infected was not discovered.

The first outbreak reported in America was the Boston epidemic of 1911, which involved fourteen hundred persons living in good residential sections of Boston and neighboring towns. It was studied by Winslow with the full coöperation of the dairy involved. It was found that 70 per cent of the cases occurred in the area of distribution of one branch of the dairy, while the customers supplied by a second branch of the same dairy escaped infection. Nine other large epidemics have since been reported and extensively studied. Limited epidemics of sore-throat due to infected milk are believed to be far more common than is indicated by published reports, for in the smaller centers of population where laboratory facilities are not readily available they attract less notice and are less likely to be reported.

Bacteriology.—Streptococci which are definitely hemolytic are frequently isolated from the throats of persons ill from epidemic sore-throat and also from the infected milk. These organisms closely resemble *Streptococcus pyogenes* and are pathogenic for rabbits. *Streptococcus lacticus,* which is always present in milk, is non-hemolytic and is non-virulent for man and rabbits.

Streptococcic infections are relatively common both in man and cows. A milk handler may readily infect milk through coughing or sneezing. Such

contamination can account for an acute epidemic of several weeks' duration only when the infected milk handler continues at his work, which is unlikely unless he be a healthy carrier.

It is apparent that there must be some continued source of infection which is related to the milk supply. Mastitis or garget is not uncommon in cows. *Streptococcus lacticus* or closely related strains are the common cause. Were these pathogenic to man, milk would be almost constantly infected by milk handlers, which is not the case. In five of the American epidemics a virulent *Streptococcus hemolyticus,* distinct from the bovine types of streptococcus, has been recovered from the infected milk. Davis found these practically identical with the cocci isolated from septic sore-throat cases.

Davis and Capps have shown that hemolytic streptococci from sore-throat produce mastitis when injected directly into the cow's milk ducts. This mastitis may be severe, leading to caked bag, or the organism may grow and multiply in the milk ducts without producing visible changes in the udder. Cows so infected produce milk which contains hemolytic streptococci and an increased number of leukocytes. These infections may persist over a long period in the form of chronic mastitis. These workers found that swabbing the streptococci around the meatus of healthy teats did not produce an infection, but if the teat were scarified an ascending infection occurred marked by an increase in the number of leukocytes and the presence of large numbers of streptococci in the milk. The organisms were still present at the end of four weeks.

One is led to conclude that the causative organism is a human strain of streptococci which reaches the cow's udder probably through the hands of a milker coming in contact with an abrasion on the teat. Subsequently the milk from this cow infects the entire quantity of milk marketed.

These streptococci retain their viability in milk, cream and milk products. Ice cream especially has been found to preserve the organisms for at least three weeks without appreciable diminution in number or virulence. Cream contains more organisms than milk, since the bacteria cling to the fat globules. The organisms survive the flash method of pasteurization, but cannot withstand the usual method of pasteurizing at 145° F. for thirty minutes.

Several years ago an epidemic of septic sore-throat among over sixty guests and employees in a large summer hotel came under the personal observation of the writer. A thorough study of the situation was made by the epidemiologist of the State Department of Health. The outbreak was finally traced to the milk supply and a milker was discovered who had a boil on his wrist. After this milker was removed from the dairy and the milk

supply pasteurized no further cases appeared. Here the infection did not start from a cow but from a human carrier.

Epidemiology.—The outbreaks are seasonal, occurring during the winter and spring. They are explosive in character, several members of a household often being stricken at the same time. The disease runs a course of one to three weeks. In most epidemics the relationship to the milk supply seems definitely established. Further studies may show that other media may serve to convey the disease. Secondary contact cases occur, but are few in comparison to the original infection.

Incidence.—*Age and Sex.*—Winslow found that children were less frequently affected than adults and that infants were almost free from the disease. Children of school age furnished a comparatively small number of cases, while young adults between sixteen and forty-five comprised more than half of the total. The gravity of the disease increased with advancing years, with two-thirds of the deaths in persons above fifty-five. He found that 71 per cent of his cases were females. Nursing babies and children who have only pasteurized milk escape. Natural resistance plays its part in protecting children and it is thought that men may escape more often because they are less frequently milk drinkers than women.

Signs and Symptoms.—The *incubation period* is short—from one to three days. The *onset* is sudden, with malaise, chills, dull headache and sometimes nausea and vomiting.

The patient complains of painful swallowing and on inspection the tonsils and pharynx are congested and red. After a few hours an exudate appears on both tonsils. This is usually thin at first and has a gray or yellowish color. It may present the appearance of a membrane resembling that of diphtheria. It is confined to the tonsils and does not have any tendency to spread. Swallowing may be extremely painful for days.

The constitutional symptoms may be severe, with the temperature rising to 103° or 104° F. The pulse is accelerated and there is much weakness and prostration. This lasts for two or three days, at which time the exudate on the tonsils has disappeared.

Enlargement of the cervical glands is a very frequent accompaniment of this disease. Adenitis may appear early or after several days. The glands may be considerably swollen and very tender to the touch, but very rarely go on to suppuration. They may be palpable for weeks after the acute attack. A skin eruption is frequently present. It may be erythematous and closely resemble the rash of scarlet fever or may show small hemorrhagic spots.

In mild cases the acute symptoms subside in from three to five days but complications are common and relapses frequently occur, especially a recurrence of the tonsillitis after an interval of a week or ten days.

Complications.—The most important complications are enlargement of the cervical lymph-nodes, erysipelas, otitis media, bronchopneumonia, arthritis, pleurisy, nephritis and endocarditis. Peritonitis where postmortem shows no evidence of an appendicitis or intestinal perforation is a part of the general septicemia. It has been noted in most of the epidemics and is one of the most frequent complications.

The persistence of foci of streptococci which later flare up accounts for the arthritis, muscular rheumatism and endocarditis. Blood cultures in severe cases show the presence of streptococci. The cases occurring in an epidemic are apt to have more frequent and more serious complications.

Diagnosis.—The diagnosis of the individual case may present some difficulty until the explosive nature of the outbreak is recognized. Cases are found among those who are patronizing a certain milk dealer or who go to the same restaurants or ice cream parlors.

The glandular swelling, extreme swelling and soreness of the throat, the marked prostration and recurrence of sore-throat after a drop in the fever, differentiate the condition from ordinary tonsillitis.

Appendicitis with rupture may be suspected when peritonitis occurs, but a laparotomy will reveal a peritonitis with the appendix intact.

Scarlet fever is not easily differentiated if the rash is severe, but the blanching test is negative and there is no strawberry tongue and the rash appears on the third or fourth day.

Prognosis.—The mortality in recent epidemics ranges from 2 to 5 per cent. The disease takes its heaviest toll from those over fifty-five years of age. Peritonitis is the most common cause of death.

The disability in mild cases continues from nine to ten days, but relapses and complications may prolong the disease indefinitely.

Prophylaxis.—Present evidence indicates that efficient pasteurization of milk and milk products, including cream and ice cream, will protect the consumer from streptococcus infection. The cocci cannot withstand the "holding" by which the milk is kept at a temperature of 145° F. for thirty minutes. The flash method is not effective. Certified raw milk is not proof against streptococcic infection, as was shown by the Boston epidemic.

Every case of septic sore-throat should be isolated with as much care as one of diphtheria or scarlet fever.

Treatment.—Children who may only present mild symptoms should be kept in bed until all constitutional and local symptoms have disappeared. Small doses of aspirin or phenacetin can be given to relieve the pain and fever. Some physicians claim excellent results from the use of methenamin in the first two or three days. To produce sleep and to quiet the restlessness, allonal or amytal can be employed even in very young children. It is doubt-

ful if the benefit which may possibly result from the use of antistreptococcus serums is worth the pain and discomfort of the injection.

Local irrigations of the nose, pharynx and throat with large quantities of hot normal salt solution are of great benefit and are not disturbing to the child. Spraying or directly applying weak solutions of argyrol, mercurochrome, gentian-violet, etc., is of decided advantage in shortening the attack and relieving the throat. Older children can gargle with mild antiseptics or a saline solution.

The inhalation of hot vapor or steam impregnated with benzoin, eucalyptol, etc., is very soothing.

The ice bag or collar kept constantly around the throat gives more relief than any other treatment when the cervical glands are involved.

If diphtheria is suspected the use of diphtheria antitoxin is advised so that no time may be lost pending the report of the bacteriological examination.

Public Health Regulations.—The Sanitary Code of the New York State Department of Health includes septic sore-throat among the communicable diseases that must be reported to the local health officer. The report must be made within twenty-four hours from the time the case is first seen by the physician. Children suffering from this disease are excluded from school and gatherings. The length of time and other conditions are prescribed by the local health authorities.

This disease is summarized in the report of a committee of the American Public Health Association.

1. INFECTIOUS AGENT.—Streptococcus (hemolytic type).

2. SOURCE OF INFECTION.—The human nasopharynx, usually the tonsils, any case of acute streptococcus inflammation of these structures being a potential source of infection, including the period of convalescence of such cases. The udder of a cow infected by the milker is a common source of infection. In such udders the physical signs of mastitis may be absent.[1]

3. MODE OF TRANSMISSION.—Direct or indirect human contact; consumption of raw milk contaminated by case or carrier or from an infected udder.

4. INCUBATION PERIOD.—One to three days.

5. PERIOD OF COMMUNICABILITY.—In man, presumably during the continuance of clinical symptoms; in the cow, during the continuance of discharge of the streptococci in the milk, the condition in the udder tending to a spontaneous subsidence. The carrier stage may follow convalescence and persist for some time.

6. METHODS OF CONTROL

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[1] Mastitis in the cow, due to bovine streptococci, is not a cause of septic sore-throat in humans unless a secondary infection of the udder by a human type of streptococcus takes place.

(*a*) The infected individual and his environment

1. *Recognition of the Disease.*—Clinical symptoms. Bacteriological examination of the lesions or discharges from the tonsils and naso-pharynx may be useful.

2. *Isolation.*—During the clinical course of the disease and conva-lescence, and particularly exclusion of the patient from participation in the production or handling of milk or milk products.

3. *Immunization.*—None.

4. *Quarantine.*—None.

5. *Concurrent Disinfection.*—Articles soiled with discharges from the nose and throat of the patient.

6. *Terminal Disinfection.*—Cleaning.

(*b*) General measures

1. Exclusion of suspected milk supply from public sale or use, until pasteurized. The exclusion of the milk of an infected cow or cows in small herds is possible when based on bacteriological examination of the milk of each cow, and preferably the milk from each quarter of the udder at frequent intervals. Exclusion of human cases or carriers from handling milk or milk products.

2. Pasteurization of all milk.

3. Education in the principles of personal hygiene and avoidance of the use of common towel, drinking and eating utensils.

CHAPTER XVIII

GLANDULAR FEVER

Definition.—Glandular fever is an acute infectious disease, characterized by rapid enlargement of the cervical glands and a less constant enlargement of the spleen, liver, axillary and other glands, accompanied by an absolute increase in the mononuclear blood-cells.

Synonyms.—Acute epidemic infectious adenitis, infectious mononucleosis; Drüsenfieber; fièvre ganglionnaire.

History.—The disease is comparatively rare and usually occurs in small epidemics although numerous sporadic cases are on record. It was first described by Pfeiffer in 1889 under the name of Drüsenfieber. Since that time various epidemics have been reported. The disease has occurred in England, the United States, Europe and China. In 1921 the careful cytological studies of Tidy and Marsh called attention to the characteristic blood changes which serve to fix the disease as a clinical entity.

Etiology.—The infectious nature of the disease points to a common etiological factor, the nature of which is obscure. It seems most likely that it is due to microörganism or filtrable virus which gains access by way of the upper respiratory tract, since a mild catarrh is usually present. The disease is somewhat contagious, but apparently intimate contact is required for its transmission and receptivity is limited. The older writers were reluctant to cede to glandular fever the dignity of a disease entity, but the symptom-complex described in the different epidemics is characteristic of a general infection with characteristic manifestations; *i.e.,* it occurs in epidemic form, runs a self-limited course and shows involvement of the liver, spleen and kidneys as do other acute infections.

Attempts have been made to establish its relationship with other infections. Stalberg describes an epidemic of glandular fever which occurred two months before an outbreak of influenza in the same locality and considers the possibility of some connection between the two. An unknown etiology is the main point in common. The glandular enlargement, lymphocytosis and lack of pharyngeal and respiratory involvement are in marked contrast to influenza which rarely shows glandular enlargement but does show acute inflammation of the upper respiratory tract and pharynx and a leukopenia.

Glandular fever has more points in common with pestis minor, a bacteriological variation of pestis major, which is observed to precede and fol-

low epidemics of the plague. In both lymphadenitis is the local manifestation
although in glandular fever the cervical glands are the first involved and
the inguinals secondarily, while in plague the inguinal glands are involved
in 70 per cent of the cases and the cervical and maxillary glands rarely. In
both the incubation period is from five to seven days, the course is mild and
the prognosis favorable. In plague *Bacillus pestis* is found readily in the
glandular tissue and blood smears while no organism is found in glandular
fever. Guthrie and Pessel considered the possibility of a relationship with
dengue fever since the preparatory school in which they studied an epidemic
of glandular fever drew students from vicinities in which dengue fever was
prevalent at the time (1922). Points which the two diseases have in com-
mon are: (1) Short prodromal period; (2) sudden onset with chilly sensa-
tions; (3) short, sharp febrile course; (4) headache, lassitude, general
malaise; (5) frequent enlargement of the spleen; (6) an enlargement of the
lymph-nodes which persists; (7) cessation of the epidemic with the onset of
cold weather and the disappearance of mosquitoes; (8) favorable outcome.
Glandular fever differs from dengue in: (1) Lack of skin rash; (2) no
breakbone sensations and no pain in the loins; (3) involvement of the post-
cervical glands rather than the inguinal as in dengue fever; (4) initial
leukocytosis rather than the leukopenia of dengue; (5) peculiar appearance
of the throat in many cases; (6) greater morbidity among the younger chil-
dren which is not the case in dengue fever.

Gilbert and Coleman considered the possibility of its relationship with
tularemia and with Malta fever as there is a slight resemblance in symptoms.
Blood was obtained from two adults, both of whom had recovered from
an illness reported to be glandular fever. Both serums were tested with
agglutinins for *B. tularensis* and *B. melitensis* with negative results. Long-
cope obtained negative results in the Widal, von Pirquet and Wassermann
reactions.

Bacteriological examinations have proved inconclusive. In all cases
throat symptoms are slight in comparison to the marked enlargement of the
postcervical glands. Tonsillitis is not associated with glandular fever and
pharyngitis does not progress beyond a slight reddening. Streptococci have
been found in the throats of patients many times but in view of the fre-
quency with which streptococcus is found, this is not conclusive. Gilbert
and Coleman isolated *Streptococcus hemolyticus* from four throat cultures
and from one specimen of pus. Streptococci producing methemoglobin were
isolated from six throat cultures.

Influenza bacilli and staphylococci have also been found.

Pathology.—The favorable outcome of glandular fever results in a
lack of necropsy records. A biopsy of an enlarged gland was reported by
Longcope as follows:

"From the left axilla the lymph node has been excised. This, on section, shows almost complete loss of normal structure. There is marked lymphoid hyperplasia of the germinal centers, the cells of which show karyorrhexis and karyokinetic nuclei. In the lymph spaces between the cords there is active proliferation of the epithelioid cells of the reticulum with the formation occasionally of large uninuclear cells almost of giant size. A few of these large epithelioid cells are also mixed with the cells in the lymph cords. Occasionally an eosinophilic leucocyte is seen. The picture suggests very strongly Hodgkin's disease though one would scarcely dare to make a definite and positive diagnosis."

Hematology.—The hematology which is an important part of the picture was first studied extensively by Tidy and Morley and since then has received careful study by several investigators. A moderate leukocytosis may be expected at the beginning of the attack and a lymphocytosis at some stage of the disease. The lymphocytosis apparently exists for some time after recovery from the disease. The above observers found that the lymphocytes made up 74 per cent of the white blood-cells on July 1, 1920, the percentage rose to 84.6 per cent on July 5, gradually fell to 50.4 per cent on September 15, and on January 8, 1921, was 38.2 per cent.

The leukocytosis depends upon a relative and an absolute increase in the mononuclear cells. Three types of mononuclear cells are found:

1. A small mononuclear leukocyte identical with the small leukocyte of normal blood.

2. Large mononuclear cells identical in appearance with the large mononuclear and transition cells of the normal blood.

3. Mononuclear cells of a type not usually encountered in normal blood. These are larger than the small lymphocytes and contain oval, kidney-shaped, slightly lobulated, or Rieder typed nuclei, staining deeply in Wright's or Hasting's stain. They were usually without nucleoli, and were often eccentrically placed in the cells. It was difficult at times to differentiate these on one hand from small lymphocytes and on the other from large mononuclear cells. A negative oxydase reaction differentiates these from myeloid cells and they are believed to be of lymphatic origin.

During convalescence the abnormal cells gradually disappear from the blood. There is a slight increase in eosinophils. The erythrocytes and hemoglobin remain normal.

Occurrence.—Glandular fever is essentially a disease of childhood, occurring chiefly among children from one to ten years of age, and in general the younger children are more susceptible than the older ones. In an epidemic occurring in central New York, Gilbert and Coleman studied the in-

cidence according to family groups and found that thirty-nine of the forty-three children in these families, or 90 per cent, developed glandular fever, while fifteen of the thirty-two adult contacts, or 46.8 per cent, were affected. In some outbreaks adults have been the principal sufferers. Terflinger reported an epidemic in the Northern Indiana Hospital for the Insane of 150 cases, all adults, who ranged in age from eighteen to eighty years.

Symptoms.—The *incubation period* is from five to ten days, usually about seven days.

The *onset* is usually sudden, with chilliness, malaise, headache, muscular soreness, sore-throat and pain in the neck, especially on motion. Pain upon swallowing and redness of the throat, coryza and a granular conjunctivitis occur in some cases. Nausea and vomiting, loss of appetite and diarrhea or constipation may be present.

The *temperature* rises rapidly from 102° to 104° F. and continues high for from two to seven days and then falls either by lysis or crisis. The pulse is correspondingly rapid, of poor quality, and the respirations are increased.

Enlargement of the cervical lymph-nodes occurs early in the disease, usually by the second day. The glands along the posterior border of the sternocleidomastoid muscle become enlarged and tender. The swelling may reach the size of a pigeon's egg. These tender and enlarged nodules cause the child to hold his head somewhat rigidly. The affected nodes remain discrete and form a chain along the border of the muscle. The enlargement often begins on the left side at the angle of the jaw and may not become bilateral for several days.

Gland groups other than those in the neck may be involved, particularly the axillary and inguinal nodes, and substernal pain, spasmodic cough and difficulty in swallowing suggest that the bronchial and retro-esophageal glands may be enlarged. The spleen is often palpable and the liver may be enlarged. Abdominal pain sometimes occurs.

The disease reaches its height in about four days. The temperature may subside slowly or a crisis, accompanied by severe sweating, may occur. The glandular swelling may immediately subside or it may persist for a month or more.

During an epidemic cases occur with symptoms so mild as to escape notice under ordinary circumstances, a fact which suggests that glandular fever may be more frequent than it is now considered.

Diagnosis.—The diagnosis should offer few difficulties; the characteristic features are (1) swelling of the lymph-nodes and pronounced fever without obvious cause, (2) the disproportion between the degree of cervical adenitis and the catarrhal symptoms, (3) the increase of mononuclear leukocytes in the blood, (4) the characteristic position of the head, (5) the

mild course of the disease, (6) and its usual occurrence in children or young adults. Mumps should offer few difficulties in differentiation, especially as the parotid glands are not involved. Acute lymphatic leukemia may be excluded by the mild course, absence of hemorrhages, moderate leukocytosis and the presence of many white cells with bilobed nuclei.

Prognosis.—This is excellent. Death never occurs unless there are serious complications. Among ninety-six cases reported by West there was only one death and that occurred in a very delicate child who had recently recovered from scarlet fever.

Treatment.—*Preventive.*—Isolation of affected children after as early a diagnosis as possible is desirable. Little is known of the etiology of this disease although it appears to be a streptococcic infection with the tonsils as the point of entry. Fortunately the disease is not common and epidemics are few in number. Pfeiffer pointed out the contagiousness of the disease in a single family or house and that it rarely extended beyond. There is no house-to-house infection and rarely does it spread through a school. Closure of a school where one or more cases have appeared would accomplish nothing in the way of prevention. When it appears in a family it usually attacks all of the young children.

Medical.—Treatment is purely symptomatic. The intestinal tract is generally disturbed. When the initial vomiting has ceased give the child light and liquid diet. The child should be confined to bed during the febrile stage. A cathartic should be given at once in order to thoroughly cleanse the bowels. Calomel in small doses is most effective.

There is no specific internal medication. During the febrile period when there is great discomfort and restlessness a combination of aspirin, phenacetin and caffein in small doses gives relief. Salol or quinin in fairly large doses is recommended by some authors. All treatment should be directed to insure the comfort of the patient as the disease itself is self-limited.

The pain from the enlarged glands may be greatly relieved by external applications. The use of poultices, hot fomentations or a hot water bottle gives more comfort to young children than ice applications. Cold compresses of magnesium sulphate have been recommended. Suppuration of the glands need not be feared as it is an extremely rare sequela.

The complications can be treated as they arise. Epistaxis is severe in some cases and the nostrils will require packing.

There may be anemia, loss in weight and depression. Tonics are indicated such as iron, small doses of Fowler's solution, syrup of hydriodic acid, malt, cod-liver oil, etc.

The child will be completely restored to health in from four to six weeks after the initial symptoms.

The Sanitary Code of the New York State Department of Health requires that whenever there shall occur in any municipality an outbreak or an unusual prevalence of glandular fever it shall be the duty of the physician to notify the health officer who shall report to the State Department of Health.

CHAPTER XIX

ERYTHEMA INFECTIOSUM

Definition.—Erythema infectiosum is a mildly communicable disease appearing in various forms but occurring chiefly in children. The infective agent is unknown, as is the method of propagation. The constitutional symptoms are slight, the eruption being the characteristic feature. It is without complications or sequelæ.

Synonyms.—The literature abounds in reports of small localized epidemics of a disease characterized by an erythematous rash which it would seem could be grouped under the term "erythema infectiosum." Various authors, however, in describing a particular epidemic or group of cases have used the following terms: roseola infantum, oerliche Roetheln, megalerythema epidemicum, Grossflechen, exanthema variable, erythema infantum febrile, epidemischer scarlatinosa, exanthem subitum, toxic erythema, critical preëruptive fever.

History.—The first reports of epidemics of the disease are found in the German literature. Tschamer in 1886 gave an account of the eruption and clinical history and felt he was dealing with an atypical or abortive type of German measles. For that reason he proposed the name "oerliche Roetheln." Escherich studied two epidemics in Gratz and one in Vienna and was the first to claim it was not identical with German measles but was a separate and distinct entity. Schmid, one of his assistants, wrote an exhaustive description of the disease based on a study of 121 cases.

The first to propose the term erythema infectiosum was Stickler of Giessen who, in 1899, described an epidemic of forty-five cases. Escherich at once accepted this name and urged its acceptance.

Pospischill, when in charge of the contagious pavilions of the Wilhelmina Children's Hospital in Vienna, reported an unknown eruptive disorder as "ein neues als selbständig akannta akute Exanthem." He differentiated it from German measles, scarlet fever and measles. In a later article he stated that the cases formerly described by him were in reality erythema infectiosum. This term is now in general acceptance among German and Austrian writers.

An epidemic which appeared in several places in Switzerland in 1916 was reported by Weber who stated he was convinced from his study of the literature that the cases he studied corresponded in all the essential features

to those described as erythema infectiosum. A small epidemic of thirty-eight cases was reported in Breslau in 1913 and an article appeared in the *Münchener medizinische Wochenschrift* in 1917 by Ochsenius describing an outbreak of this disease.

In 1900 Dukes in England described several epidemics of an eruptive disorder, to which he applied the term "fourth disease," but his claim of its clinical entity has not been generally accepted. Filatow reported a similar epidemic in Russia many years before. There is a marked similarity in the descriptions given by these two authors and there is therefore possibly some relation between fourth disease and erythema infectiosum. Although there have as yet been no epidemics in this country described under this term, they have undoubtedly occurred but have been reported as unusual and atypical forms of the common exanthemata. For example, Braner of Hamburg, New York, in a personal communication reported a series of thirty-three cases, twenty of which were females and thirteen males. All but two of the female cases were in young children. The first diagnosis was scarlet fever but a careful analysis and study of the cases by an experienced dermatologist and a competent pediatrician who were called in consultation convinced these observers that the disease was not scarlet fever, measles or German measles and that it corresponded in every important detail with the course and description of erythema infectiosum.

In a textbook on *Diseases of Children* published in 1874 by Meigs and Pepper they described a toxic erythema "which is characterized by fever with headache, restlessness, and, at times, delirium, which persists from two to four, occasionally six to seven days, when the symptoms and fever terminate as an eruption makes its appearance. The eruption appears first on the face and neck and spreads to the rest of the body in 24 to 48 hours and simulates the rash of measles closely, but catarrhal symptoms are absent." This is an excellent description of cases of erythema infectiosum. Westcott of Philadelphia reported a series of cases very similar which he called pseudorubella. A series of thirty cases observed by Levy in Detroit in 1921 possessed many similarities. Veeder and Hempleman described in detail an epidemic in St. Louis in 1921 to which they proposed the name "exanthem subitum" to designate the abrupt and unexpected appearance of the rash. Similar epidemics have been reported in Ann Arbor, Michigan, and in Montreal, Canada. Herrick recently presented a most interesting article on two epidemics occurring in Cleveland. There were fifty-two cases in that city in 1924 and twenty-two in 1925, which after being studied carefully were diagnosed as the disease under discussion.

In looking over the literature one is greatly impressed with the lack of agreement as to just what constitutes the distinctive features of this disease. The nomenclature would be simplified and the atmosphere cleared

if all of these cases could be classified under the group name of erythema infectiosum.

Epidemiology.—It is difficult to make any satisfactory study of the epidemiology, as the disease occurs so infrequently. It is only feebly communicable and the susceptibility to it is not very great. The reported epidemics vary from five to one hundred cases. The outbreak in Switzerland reported by Weber occurred in an orphan asylum where only two or three cases developed each week. Coerper had eighteen cases in Barmen, of which three were in a children's home of thirty-two children and six in a child welfare station among twenty-five children from one to four years of age. None of Herrick's cases had the disease twice, although it occurred in the same locality in two successive years. It seems likely that one attack gives immunity for life. An attack of measles, scarlet fever or German measles affords no immunity against erythema infectiosum. Both sexes are equally affected. The reported epidemics were most frequent in the spring and early summer. It is not known how long the disease is infectious. Many cases are unrecognized on account of the mildness of the attack, and no physician is consulted.

Etiology.—The specific agent, mode of transmission and viability of the organism is unknown. The age most commonly affected is between four and twelve years, the youngest case reported being in a fourteen-months-old infant. The period of incubation is between five and fifteen days.

Symptoms.—The subjective symptoms are usually very mild, although there may be more or less fever, malaise, loss of appetite, coated tongue and nervous irritability for two to four days. When the general condition of the patient seems to improve an eruption develops. In other cases the rash is the first symptom noted. The external skin only is affected. No changes on the mucous membranes have been observed. While the face is not always involved, large red spots usually appear first on the cheeks, then soon coalesce and become confluent. Shortly after the rash shows on the face it is found on the body, especially over the extensor surfaces of the arms and legs and to a lesser degree on the trunk. The rash is macular, reddish in color with a bluish undertone, and fades on pressure. The eruption does not itch or feel hot to the touch. The center of the macules soon fades, but the periphery remains, giving a lacelike or geographic (maplike) appearance. The rash fades rapidly from the face and trunk, but very slowly on the arms and legs. The superficial lymph-nodes are not enlarged. There is no coryza, conjunctivitis or cough.

Weber made a careful blood analysis in his cases and invariably found a leukopenia of from 2,500 to 5,000 leukocytes, with a diminution in the proportion of polynuclear leukocytes. Veeder, Hempleman and others have confirmed the blood findings of Weber. This blood-picture must be con-

sidered one of the characteristic features of this disease and is a strong argument in favor of its specific entity.

Diagnosis.—This disease is of importance in reference to diagnosis, especially in excluding the acute exanthemata. The care and welfare of the patient and protection of other members of the family and of the community depend largely on an early and accurate diagnosis of such diseases. The expense involved in the maintenance of quarantine, the inconvenience, etc., are considerable and a great injustice is wrought when a wrong diagnosis is made and a child unnecessarily placed in seclusion.

The disease most likely to be mistaken for erythema infectiosum is German measles. The presence of the enlarged superficial lymph-nodes, the difference in the character and course of the eruption, and a slight leukocytosis would exclude this disease. In several reported epidemics, children who were known to have had rubella contracted erythema infectiosum.

Measles can be excluded by the absence of all involvement of the mucous membranes with catarrhal symptoms, of all constitutional symptoms and of Koplik spots. The appearance of the rash on the arms is strikingly similar at first glance, but further study and its later lacelike aspect should clear up the diagnosis.

The disease has been occasionally mistaken for scarlet fever, but there ought to be no difficulty in making a differential diagnosis. The throat symptoms, color, size and distribution of the rash, the severe constitutional symptoms with a high temperature and rapid pulse of scarlet fever have nothing in common with erythema infectiosum.

While drug, toxic and intestinal rashes are very similar to the eruption of erythema infectiosum, the specific cause and the duration, location and course of the eruption should remove any possibility of confusion. The same can be said of urticaria, where the absence of itching and the characteristic wheal formation make the diagnosis clear.

Several diseases of the skin, such as erythema exudatum multiforme and pityriasis rosea, present some similarities, but a careful study of the appearance, course and location of the skin lesions will serve as a guide.

Treatment.—Before the appearance of the rash the symptoms point to some slight digestive upset. Rest in bed, the use of some mild laxative and a restricted diet are all that is necessary. The temperature can be controlled by cold sponges and an ice-cap or by small doses of aspirin, phenacetin or aconite. When the rash appears a simple dusting powder can be used or the patient may be sponged with a solution of bicarbonate of soda, one dram to the pint, a saturated solution of boric acid or a weak solution of alcohol and water (1 : 10).

As the period of contagiousness is not known, it is wise to keep the child in quarantine until the eruption has disappeared.

CHAPTER XX

RABIES

Definition.—Rabies is an acute, specific, communicable disease to which all mammals are susceptible, but in settled communities it is confined largely to dogs. It is usually conveyed to the human by the bite of an affected animal. The infection affects the brain, causing a rapidly fatal paralysis. Its etiology has not been definitely determined but it is known to be a filtrable virus.

Synonyms.—Hydrophobia; Tollwut, Hundswut, Wasserscheu; la rage.

History.—This disease is one of the oldest known, being described by Aristotle in the fourth century, B.C. It is said to have first appeared in America in 1768 and to have spread rapidly to all parts of the United States and Canada, where it has since been endemic. The saliva of rabid animals was shown to carry the infective agent in 1804. The name hydrophobia was given to human rabies by Celsus. Prior to Pasteur's discovery that rabies is caused by a specific virus (1884) and the publication of the classic preventive method which bears his name, there were many bizarre methods of treatment advocated, none of which proved efficacious. It is interesting to note that Celsus advised cupping and applying an actual cautery to the wound. Among some of the more modern but inefficient remedies suggested were musk and cinnabar, commonly called "tonquin" or "East Indian remedy"; ash-colored ground liverwort and black pepper; copper; suppuration of the wound for six months' continually fomenting with a pickle made of vinegar and salt; common salt and strong mercurial ointment. For a long time tetanus and hydrophobia were thought to be the same disease.

Incidence.—Rabies is said to occur in all parts of the world with the exception of Australia and several smaller islands where control measures have always been strictly enforced. No cases have occurred in Denmark, Sweden and Norway for more than half a century. Following a strict enforcement of the muzzling law and a quarantine period on all dogs imported into the country begun in 1903, England was free from the disease for many years. During the World War, however, it is said to have been reintroduced by dogs brought to the islands in flying machines.

In the United States the disease is apparently on the increase in many sections due to the lax enforcement of licensing laws and control measures.

In New York City during 1926, out of 462 dogs proved to be rabid 128 were found to be strays.

Susceptible Animals.—As has been stated any mammal may contract rabies, but dogs appear to be by far the most susceptible. It is common in cattle, sheep and goats and to a lesser degree in horses, swine and cats, and in many wild animals. In some of the southwestern states it has been reported that skunks are natural carriers of the disease.

Prevalence.—The disease is popularly supposed to be more prevalent during hot weather or dog days. This is true only in so far as dogs run at large more freely during mild weather and are thus more liable to be attacked by a rabid animal. The disease actually occurs at all seasons of the year.

Etiology.—Rabies is caused by a specific but unidentified virus, present in the saliva of the infected animal. When such an animal bites a person or another animal, the virus is carried into the deeper tissues by the teeth. It is not improbable that infection may occur if the saliva of a rabid animal enters a cut or scratch. Great care should therefore be taken in examining animals suspected of being rabid. One of the common symptoms in dogs is a paralysis of the throat muscles, causing the animal to paw his jaws as if a bone was caught in the throat. If an attempt is made to dislodge the supposed obstruction with the hand, a scratch from the teeth may result in infection.

As has been inferred, bites on the hands and face are most dangerous, particularly the latter, since the distance to the brain along the veins is short. A fatal case reported in a boy about five years of age during the year 1909 in Columbus, Ohio, is of particular interest because all factors were so closely checked. The child in question was bitten by a dog one Sunday afternoon. The teeth went through one eyelid and a portion of the eyeball. The dog was killed and its head submitted to the Ohio State Laboratory on Monday morning. By afternoon of that day Negri bodies had been demonstrated and a report made to the family physician. By night the child and its parents were on the way to a Pasteur Institute in Chicago, there being no arrangement by biological houses at that time, as there is at present, for the preventive treatment to be sent to the attending physician by mail. There was no local institute. Three weeks later, on the night the child returned home, typical paralytic symptoms developed and the child died within a few days. In this case the path from the site of inoculation to the brain was so short that it reached the brain before a sufficient immunity could be established.

It is probable that in addition to the site of inoculation the amount of infective material introduced and the virulence of the virus (the latter undoubtedly influenced by the rapidity of transfer from animal to animal) play

a considerable part in determining the question as to whether a person who has received a bite from a rabid animal will contract the disease and what time will elapse before the disease develops. The presence of large numbers of small nerves or of trunk nerves at or near the wound is known also to be a determining time factor. As indicated above some cases may develop before the Pasteur treatment can possibly confer sufficient immunity to protect the patient, while others, untreated, may go for months before symptoms appear, or may escape the disease altogether.

Only about 16 per cent of persons bitten and untreated contract rabies.

Pathology.—The virus of rabies is known to travel along the nerves or neighboring lymphatics to the brain. If portions of the cord or brain of an animal dying from rabies are inoculated beneath the dura mater of a rabbit or guinea-pig, the latter animal will succumb to the disease. In 1903 Negri demonstrated the presence of certain bodies, which have since been called Negri bodies, in the hippocampus major, or Ammon's horn and in the bulb of infected animals. Comparative tests carried out soon showed that the presence of these bodies in a suspected animal was pathognomonic for rabies.

Symptoms and Clinical Course.—*In the dog,* rabies may assume either the dumb or the furious form. In the former, the dog may show a change of disposition. Weakness develops and some form of paralysis appears, often first in the hind quarters from which it gradually spreads. The tone of the bark may be changed and the dog may act as if he had a bone in his throat as the throat muscles become affected. It is this which causes rabid animals to refuse water or other liquids, not a fear of water as the term "hydrophobia" implies. Death usually results in from three to four days after the appearance of symptoms, though longer periods have been observed.

In the furious form of canine rabies the dog's disposition changes, he becomes excited, uneasy and pugnacious, avoids water for the reasons given above and shows a tendency to run long distances (reports of from twenty-five to fifty miles are not unusual if the dog is unmolested), biting and snapping at everything in his pathway. Because of this tendency in the dog the disease may be spread with great rapidity over a large territory.

In human rabies the first symptom is usually difficulty in breathing or swallowing, the latter being particularly characteristic. Neuralgic pains may appear. Glycosuria is a common symptom, as is the pinpoint contraction of the pupils. After forty-eight hours the nervous symptoms become more pronounced. There is often insalivation and great care must be taken that the saliva, or linen soiled by it, does not come in contact with cuts or scratches on the hands or other portions of the skin of those caring for the patient. Trembling of the muscles or convulsions develop early in the course of the disease but become less frequent as the patient becomes

weaker and the paralysis spreads. There is frequently a dread of light or drafts and the eyes become fixed. The patient is usually conscious most of the time until near the end. Death is caused by the paralysis of the heart or respiratory centers. In human rabies the pulse increases to over 100 and the temperature to about 104 with morning remissions until just before death, when it rises sharply.

Diagnosis of the Biting Animal.—For a diagnosis of rabies laboratory tests are essential. Formerly the test for rabies in man or animals was made by inoculating a portion of the brain beneath the dura mater of a rabbit, but as in the laboratory animal from two and one-half to several weeks elapse before symptoms develop, it is not of much value in deciding whether a person bitten by a suspected dog should take the Pasteur treatment. It is used, however, where the results of the Negri method are doubtful. This test has therefore been practically replaced by the Negri method before mentioned. In a positive case the Negri bodies can be demonstrated in smears or spreads made from the fresh brain or from sections of the Ammon's horn, and are considered absolutely diagnostic for rabies.

The brain, however, must be fresh. Far too often the head of a suspected dog is shipped to the laboratory without being packed in ice with the result that the brain is frequently too decomposed to be of any value for the test.

Examinations for Negri bodies are made from smears, spreads or sections. Usually paraffin sections are not necessary, for if present in any quantity the Negri bodies are usually easily found by one of the first two methods. In making smears, a cross section of the Ammon's horn is pressed several times against the different portions of the surface of a clean microscopic slide, which after air drying is then fixed for ten seconds in neutralized methyl alcohol containing 0.1 per cent of picric acid stained with a solution made up of a saturated solution of fuchsin 0.5 part, saturated solution of methylene-blue 10 parts, and distilled water 30 parts. Spreads are made by taking portions of the Ammon's horn, cerebellum or cerebral cortex and pressing between a cover glass and slide. The smears are then fixed and stained in the same manner as described for smears.

At the time the suspected animal's head is received, a portion of the brain should be placed in neutral glycerin and set aside in the ice box for inoculation tests, should the latter become necessary. The glycerin tends to kill off putrefactive organisms without materially affecting the rabies virus.

Prognosis.—Once symptoms of rabies have developed in a human the case is practically hopeless. For this reason it is of the greatest importance to have a diagnosis made as soon as possible after a person has been bitten by a suspected dog. It is a mistake to kill the animal which has inflicted the wound unless unmistakable symptoms of rabies are apparent, for if the

dog was capable of conveying the disease at the time of biting he will develop symptoms within a week or two weeks at the most and usually within three or four days. If killed too soon, Negri bodies may not have had time to develop and the slower animal inoculation test will have to be relied upon.

The virus of rabies after entering the body travels along the nerve-fibers or the lymphatics immediately surrounding them until it reaches the brain. Thus the site of the wound is a matter of a great deal of importance. The farther it is away from the head the greater the time required for it to reach the brain and consequently the greater the chance for the preventive treatment to take effect and produce the required amount of immunity. Bites through the clothing are less dangerous than those on the exposed skin, as the saliva is to a large extent wiped off as the teeth pass through cloth.

TABLE XXXVI.—DEATH RATE FOR RABIES PER 100,000 POPULATION OF THE UNITED STATES DEATH REGISTRATION AREA OF NEW YORK STATE FROM 1915 TO 1925

Year	United States Registration Area	New York State	New York City	New York State Exclusive of New York City
1915	0.1	3	1	2
1916	0.1	2	1	1
1917	0.1	5	3	2
1918	0.1	..	..	..
1919	0.1	7	5	2
1920	..	3	1	2
1921	0.1	4	3	1
1922	..	1	1	..
1923	0.1	4	3	1
1924	..		..	..
1925	..	1	1	..

Local Treatment.—Local treatment consists in first cleansing the wound, producing bleeding and then cauterizing with fuming nitric acid. This should be done within twenty-four hours after the bite. It is best applied drop by drop from a capillary pipet. Other cauteries such as iodin have been recommended but none have been found as efficient. The actual cautery is effective on such surfaces as it touches, but fuming nitric acid, being a fluid, reaches deep crevices that the cautery will not touch. Contact of the acid with bony, cartilaginous or bloodless parts should be avoided. For these parts use pure carbolic acid.

Prophylactic Treatment.—If suspicious symptoms of the disease develop in the biting animal, or if Negri bodies are found in the biting animal's brain, treatment by the Pasteur method or one of its modifications should be started without delay. Formerly this necessitated going to a Pas-

teur institute, but in recent years the treatment can be obtained at short notice by telegraphing to one of the commercial biological houses. The treatment can be given by any practicing physician by closely following directions. The Pasteur treatment and all of the modifications depend on the attenuation by various means of the virus obtained from infected rabbits. The first injection is of virus of greatly lowered virulence. This is followed on each subsequent day with virus of gradually increasing strength, as the body gradually produces immune bodies. The ordinary course of treatment takes about twenty-one days, the emulsified cord being inoculated daily in the order in which the material is supplied by the laboratory. A form of intensive treatment which materially shortens the time of treatment is recommended where the bites are multiple and particularly if they are on the face.

The Pasteur treatment is indicated under the following conditions:

When persons have been bitten by animals which have been proved rabid either by clinical symptoms, or by microscopic examination of the brain.

When hands or face have been contaminated with saliva of a rabid animal without being bitten. This is because of the possible presence of cracks, hangnails or other small open wounds.

When persons have been bitten by stray dogs which cannot be located. The treatment is given as a precautionary measure.

When persons have been bitten, pending the laboratory diagnosis on the brain of the biting animal, provided that the symptoms or actions of the animal were suspicious, or when rabies infection of the animal cannot be ruled out.

Results of Pasteur Treatment.—The Pasteur treatment and the accepted modifications of this method usually confer immunity, provided the location of the wound is not on the face. The quicker treatment is started after the biting animal has been pronounced rabid, the greater the chance of producing an immunity before the virus reaches the brain. Intensive treatment should be given if the bites are lacerated or if on the hand or face, particularly the latter.

A great deal of research has been conducted with the purpose of perfecting a single dose vaccine for dogs. While the results show some degree of success, Moore feels that they do not justify health officers in relying solely on this method of control. He advocates also a rigid quarantine of all dogs where rabies is known to exist.

Public Health Regulations.—The Sanitary Code of the New York State Department of Health contains the following in regard to the preven-

tion of rabies and outlines the duties of the attending physician and the local health officer when a case of rabies is suspected.

It shall be the duty of every physician to report immediately to the local health officer the full name, age and address of any person under his care or observation who has been bitten by an animal having rabies or suspected of having rabies.

If no physician is in attendance and the person bitten is a child, it shall be the duty of the parent or guardian to make immediately such report. If the person bitten is an adult, such person shall himself make the report, or, if incapacitated, it shall be made by whoever is caring for the person bitten.

It shall be the duty of every person having knowledge of the existence of an animal apparently afflicted with rabies to report immediately to the local health officer the existence of such animal, the place where seen, the owner's name, if known, and the symptoms suggesting rabies.

The local health officer shall forthwith report to the state department of health the name, age and address of every person bitten by an animal having rabies or suspected of having rabies, and all the pertinent facts relating to any animal found to have or to have had rabies.

Every health officer shall confine or cause to be confined under his immediate observation any animal suspected of having rabies and shall continue such confinement for such time as may be necessary to determine the diagnosis. If an animal is known to have rabies it shall be killed under the direction of the health officer. If an animal suspected of having rabies can not be secured or confined the health officer shall authorize the killing of such animal.

Whenever any animal that has rabies or any symptoms of rabies, dies or is killed, it shall be the duty of the health officer to cause the head of such animal to be removed and sent immediately properly packed with a complete history of the animal since first suspected of having rabies to a laboratory approved by the public health council for the examination of such heads.

The local health officer may cause any animal that is of a species subject to rabies, and that has attacked or bitten any person or that in his judgment is vicious and unsafe to be at large, to be confined upon the premises of the owner of such animal, or if it is impracticable to secure and confine such animal, or if the ownership can not readily be determined, he may cause it to be killed.

The Committee on Standard Regulations for the Control of Communicable Diseases of the American Public Health Association reported the following summary of our present knowledge of rabies.

1. INFECTIOUS AGENT.—Unknown.

2. SOURCE OF INFECTION.—Saliva of infected animals, chiefly dogs.

3. MODE OF TRANSMISSION.—Inoculation with saliva of infected animals through abrasion of skin or mucous membrane, almost always by bites or scratches.

4. INCUBATION PERIOD.—Usually two to six weeks. May be prolonged to six months or even longer.

5. PERIOD OF COMMUNICABILITY.—For fifteen days in the dog (not known

in man) before the onset of clinical symptoms and throughout the clinical course of the disease.

6. METHOD OF CONTROL

(a) The infected individual and his environment

1. *Recognition of the Disease.*—Clinical symptoms, confirmed by the presence of Negri bodies in the brain of an infected animal, or by animal inoculations with material from the brain of such infected animal.

2. *Isolation.*—None if patient is under adequate medical supervision, and the immediate attendants are warned of possibility of inoculation by human virus.

3. *Immunization.*—Preventive vaccination after exposure to infection by inoculation.

4. *Quarantine.*—None.

5. *Concurrent disinfection* of saliva of patient and articles soiled therewith.

6. *Terminal Disinfection.*—Thorough cleaning.

(b) General measures

1. Muzzling of dogs when on public streets, or in places to which the public has access.

2. Detention and examination of dogs suspected of having rabies.

3. Immediate antirabic treatment of people bitten by dogs or by other animals suspected or known to have rabies, unless the animal is proved not to be rapid by subsequent observation or by microscopic examination of the brain and cord.

4. Annual immunization of dogs where the disease is prevalent.

CHAPTER XXI

TUBERCULOSIS IN CHILDREN

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INTRODUCTION

Juvenile tuberculosis presents an interesting challenge to the medical profession. For years a constant warfare has been waged against tuberculosis and a satisfying result has been obtained in reducing the mortality from this source. The greater portion of our efforts, however, has been directed against the adult type of the disease, while the juvenile type has been relatively neglected; even in view of the fact that tuberculosis in adults is the aftermath of childhood infection, in the great majority of cases! Instead of attacking the evil at its source we have allowed it to flourish as a constant menace to our people. The startling drop in the death rate of all forms of tuberculosis from 213 per 100,000 in 1905 to 94 per 100,000 in 1925 has, in a measure, acted as a sop to our vanity and stifled a demand on the part of the general public for more complete protection against the white plague. To continue along present lines would require untold years to bring the disease thoroughly under control. With the hospitalization of the active cases there has been a marked reduction in the sources of infection and this has been the main factor in reducing the incidence of tuberculosis in children, but it has been only an incidental result and not obtained by direct campaigning against juvenile tuberculosis.

Tuberculosis was recognized long before medicine became a science. In the earliest medical records of Hippocrates and Galen we find excellent clinical descriptions of advanced cases. Franciscus Sylvius (1614-1672) noted the main symptoms of the disease, such as wasting, cough, spitting of pus, and a hectic fever. He attributed the disease in most cases to pleurisy ending in suppuration. Richard Morton (1635-1696) first associated phthisis with lymphatic swelling. Bayle (1774-1816) was first to use the terms "miliary" and tuberculous "diathesis." In 1862 Villemin published his work on the experimental production of tubercles in animals. Finally in 1882 we have Koch's epoch-making discovery of the tubercle bacillus. For two thousand years the disease was considered incurable and until modern times heredity was regarded as the chief cause.

Until the beginning of the twentieth century we find practically no mention in the literature of juvenile tuberculosis. The reason for this seems quite clear. In the adult, the clinical signs and symptoms of tuberculosis lend themselves readily to a proper diagnosis. On the contrary, in tuberculous infection in childhood, the reverse is the rule. Here, in the early stages, at least, the well-known characteristic manifestations found in the adult are obscure, if not entirely wanting. Consequently, for years in many cases, juvenile tuberculosis has gone unrecognized. Only recently has much emphasis been placed on tuberculosis in infancy and childhood. The diagnosis of this disease in the young is a subject of supreme perplexity, and yet far from approaching finality. Much of delicacy and many of the so-called minor ailments of children result from unrecognized tuberculosis.

Mortality statistics of infants dying in New York City from tuberculosis show a decrease from 1,191 per 100,000 in 1868 to 94 per 100,000 in 1925. These figures border on the spectacular but it is to be remembered that they deal only with fatal cases; the number of children infected must be infinitely greater, and therefore, the number of potentially acute cases is still enormous.

The recognition of juvenile tuberculosis is of paramount importance in the battle against phthisis. There are at present sufficient beds in the sanatoria to care for the active cases of tuberculosis and with the increased amount of sanatoria treatment, childhood infection has been greatly reduced. It now devolves upon us to foster the preventoria idea. Prophylactically we are confronted with the problems relating to the control of human and bovine infection. The latter is almost a negligible factor in sections where milk production is properly regulated. Tuberculin-tested herds, pasteurization, periodic examination of the handlers, rigid adherence to cleanly methods, etc., have reduced the incidence from this source to a very small percentage of the total cases of juvenile tuberculosis.

We are all aware of the high susceptibility of children to intercurrent infections and the readiness with which they contract diseases to which they are exposed. We are also all aware of the great prevalence of tuberculosis. We know that many adults have the disease in a communicable state sometimes for years before they finally get into the hands of a physician. Children are constantly coming in contact with these individuals on the street, in the trolley cars and elsewhere. We also know that milk, which makes up a large portion of the child's diet, is not infrequently a source of tuberculosis infection. Thus, it seems quite natural to conclude that during infancy and early childhood most children have at some time been exposed to tuberculosis. Due to their high susceptibility to all infections it seems probable that a large percentage of these children develop a tuberculous infection which only rarely goes on to a clinically recognizable form. This infection is, however, sufficient to stimulate specific antibody formation.

The fact that over 50 per cent of children five years of age react positively to various tuberculin tests supports such a view. It is only natural then to ask why we do not more frequently recognize this condition. The answer is an intricate one, various aspects of which we will attempt to point out in the following paragraphs.

It is first necessary for us to distinguish what we speak of as a "tuberculous infection" from tuberculosis as a "disease." We are all familiar with the latter, with its classical picture of cachexia, cough and expectoration, loss of weight, night-sweats, hemoptysis, dyspnea, fatigue, moist râles, and a hectic temperature, or perhaps its trying glandular involvements, visceral or bone manifestations. The former, on the other hand, passes many times with no symptoms other than perhaps a slight cold, sore-throat or some minor stomach upset. In infancy and early childhood much time is spent out-of-doors in the fresh air and sunshine with long hours of rest and a properly balanced nutritious diet. This is essentially the treatment of tuberculosis. Consequently in the child's normal existence the infection is conquered before it advances to a recognizable form.

Among the poorer classes under poor hygienic surroundings and improper diet we would naturally expect to find the infection going on to advanced form. From our dispensary records and work among the poverty-stricken we know this to be the case. Also in homes where the child is constantly being reëxposed by an adult member of the family suffering from active tuberculosis we find the child more liable to develop an advanced form. Human agents are the chief sources of infection and one of our greatest problems. On a large scale a survey of all suspects should be made and positive carriers instructed as to the disposal of sputa, personal hygiene, etc. Newborn infants should be removed from infectious adults as soon as possible. Calmette advocates the vaccination of newborn infants with a tuberculosis vaccine and has vaccinated more than five thousand infants born in the Charité Hospital in Paris with promising results. The treatment consisted in giving by mouth 1 centigram of a culture of attenuated tubercle bacilli. Of 564 of these patients who have been under observation for twelve to eighteen months, only two have died of tuberculosis presumably, although 231 were reared by actively tuberculous parents. Of 753 who have been under observation for a shorter period (over six months), nine have died from the disease. Of the total 1,317 infants under observation for more than six months, only 0.7 per cent have died of tuberculosis; whereas, 25 to 32 per cent is the recorded death rate for dispensaries in France. Although any definite conclusions from this study would be premature, most health officials will agree that the results already recorded indicate that Calmette's work is of great importance to public health.

The preventoria idea has already been strongly brought to the attention

of the world by the splendid results obtained in various parts of this country and Europe. Rollier is the chief advocate of this type of treatment and his disciples have proved the truth of his teaching time and again. This sort of institution is intended primarily for malnourished, underweight children who have a definite history of exposure to tuberculosis. The treatment is so arranged that these children may better cope with their handicap. Essentially it consists of adequate, outdoor life under intelligent supervision of the physical activities, mental development, and medical needs of the child. Under these conditions the necessary provisions for increasing the child's resistance are provided and he is able to live an essentially normal existence. The healthy body is not a favorable soil for the growth of the tuberculosis seed.

In order to provide these preventoria the general public must be educated to the importance of tuberculosis in children and the beneficial effects of preventoria treatment.

It is only by the demand of the people at large that such institutions come into existence and unless the average citizen understands the importance of the situation he will not raise his voice to better conditions. Therefore, an educational campaign similar to that already being waged against the adult form of pulmonary tuberculosis should be undertaken. This can best be brought about by coöperation between physicians, public health workers, teachers, clergymen and parents. The mortality rate of tuberculosis can be still further reduced if such a campaign is undertaken.

Juvenile tuberculosis is, in the main, a result of contact with active tuberculosis in adults. An investigation of all cases of the disease in New York City by Park and Krumwiede revealed the fact that less than 10 per cent of the deaths were caused by the bovine type of the bacillus. The logical deduction then is that the remainder of the cases of tuberculosis in children have been caused by the human form. To safeguard the life of the child born into a household where there is an active case of tuberculosis, it is essential that he be removed from the source of infection as soon after birth as possible. Investigation has proved that tuberculous patients whose parents were also tuberculous were not less resistant to the disease than individuals of healthy parentage, even when both parents were tuberculous. There is no hereditary constitutional predisposition to tuberculosis but the exposure to infection in tuberculous families is greater. Flugge contamination—so called droplet infection—kissing, hand-to-mouth infection, contaminated utensils, are all more commonly found in families containing an active case of tuberculosis. The resistance of children born into such conditions is as a rule continually lowered by repeated massive infection and if they do succeed in throwing it off, they grow up to become in later years the greater proportion of our active adult subjects of tuberculosis. In some

children an immunity to tuberculosis is elaborated by foci in the lymph-nodes. Children failing to be thus immunized succumb to the more or less continued progress of the initial infection. Immunization by first infection is not absolute and varies in degree. It is thought that repeated small infections confer a more permanent immunity. Children of tuberculous parents have a greater immunity than others and tend to reach quiescence or recover more rapidly than children of non-tuberculous parents. That this immunity is real is demonstrated by the decline of tuberculosis in countries or communities where it was formerly epidemic. Races which have been subject to tuberculosis for centuries have gradually built up an immunity to the disease. This hereditary evolution is very strikingly demonstrated in our southern states in the incidence of tuberculosis among negroes, a race which has been subjected to the disease for a comparative short period of years. Morbidity in the negro race is four times greater than in the white race, which has endured the scourge for centuries.

In races which have built up a resistance to tuberculosis because of repeated infection, the mother transmits antibodies to her offspring. These antibodies can be demonstrated by the complement fixation reaction for tuberculosis. This immunity lasts about three months and serves to protect the child during this short period. The placenta seems to concentrate the antibodies with a resulting higher percentage in the cord than in the maternal blood. Infants with a positive fixation reaction do not react to tuberculin. Unfortunately the infant is incapable of elaborating its own antibodies until after the eighteenth month, so the period between this time and when the immunity transferred from the mother fails to protect is the period of the greatest danger to the child.

It was formerly believed that tuberculosis was transmitted from mother to child *in utero* but this contention has been proved false time and again. The author has been able to find but two cases in the literature where the disease was unquestionably transferred from mother to offspring and in both of these the placenta was tuberculous and permitted the transfer of infectious organisms to the fetal circulation.

Laboratory tests are of great aid in the diagnosis of juvenile tuberculosis. Allergy is responsible for the reaction in both the Mantoux and von Pirquet tests. The latter is the more widely used but is not as sensitive an indicator of tuberculous infection as the former. In the von Pirquet test an area on the volar aspect of the forearm is cleaned with soap and water and then with alcohol. A drop of old tuberculin is then placed on the prepared surface and a sterile needle is used to make a superficial abrasion of the underlying skin, taking care that no blood be drawn. The same technic is followed with the control test which is usually carried out with sterile salt solution. The drops are allowed to dry in the air, which

procedure is generally complete in about twenty minutes. No dressing is applied. In the Mantoux test the area is prepared and enough old tuberculin is injected intracutaneously to raise a definite wheal. A positive reaction is indicated by an indurated area about the site of injection and usually makes its appearance within twenty-four to forty-eight hours and then gradually subsides so that at the end of a week there remains only a dark brown area to mark the site of the reaction. The cutaneous tests may be followed by a lymphangitis and a generalized reaction which is thought to be indicative of an active focus of lymph-node origin. The tests should be read on each of the three succeeding days following their application. Positive tests are indicative of infection; they do not bear any relation to activity. Negative results are found in cases that are non-tuberculous or under the following conditions:

(a) Periods of incubation of tuberculosis
(b) Periods of extension and cachexia
(c) Menstruation, pregnancy, lactation, confinement
(d) Pneumonia, grip, pertussis
(e) Intensive tuberculin treatment
(f) Following acute infectious disease

For determining tuberculosis in children the finding of the bacillus does not play the same rôle as in adults, but tuberculin testing cannot be dispensed with. Negative tuberculin tests should be repeated. From a prognostic viewpoint the importance attached to positive tuberculin reactions is as follows:

Age, Months	Per Cent	Fatal Tuberculosis Develops
1-6	75	During the first year
6-12	50	Within twelve months
12-24	25-50	Within twelve months

ETIOLOGY

The isolation of the tubercle bacillus by Koch in 1882 was of immense practical value. This definitely proved that tuberculosis was not a constitutional, but an infectious disease. It is hardly necessary for us to discuss here the isolation, morphology, cultural and staining characteristics of this organism. However, it is well to emphasize the powers of resistance of the tubercle bacillus outside the host. This resistance is relatively great. In a dark place the bacilli may remain virulent for months in moist sputum. In dry sputum the virulence is lost after ten days, while direct sunlight kills the bacillus in dust within a few days. Proper pasteurization of milk also

kills the organism. The bacillus has been found virulent in butter made from unpasteurized milk after five months. Gastric juice *in vitro* is not germicidal in ninety minutes.

The disease is widespread and prevalent in all parts of the world except in uninvaded portions such as southern Sudan. Tuberculosis has been largely responsible for the rapid decrease of the North American Indian. High mortality and morbidity rates are found among the negroes and Italians. Greatest immunity is among those who for centuries have survived the infection and propagated. Tuberculosis mortality is lowest in the Irish race.

There are two types of the tubercle bacillus in which we are particularly interested, the human and the bovine. Much has been written on the relative prevalence of these two types in juvenile tuberculosis. Until recently it has been believed that the bovine type was responsible for more than 50 per cent of the cases in childhood and the etiological factor in practically all cases of lupus vulgaris. The latter has been entirely disproved and the former greatly overestimated. Typing the bacillus is a difficult procedure, so our more recent laboratory reports are probably nearer correct.

Cobbett estimates that the bovine type is responsible for 6.5 per cent of all deaths due to tuberculosis. The bovine type undoubtedly plays a major rôle in many cases in infancy and early childhood. This belief is substantiated by the lowered mortality rate in children between the ages of one and four in cities which have enacted an ordinance requiring a thoroughly pasteurized milk supply. Winslow and Gray, after making a study of this question, state that in such cities there is a lowered death rate from tuberculosis at this age period of twenty-five deaths per 100,000. As the death rate from the disease at this age period ranges from 100 to 125 per 100,000, the death rate from bovine tuberculosis in the preschool child can be regarded as 20 to 25 per cent of the deaths due to tuberculosis. This is probably a key to the prevalence of bovine tuberculosis in children of this age. Richardson found in a survey of 368 cases in children under five years of age 292 to be of the human type and 76 to be due to the bovine type. In older children the human type is more prevalent.

One of the most important sources of infection is direct contact. This point cannot be stressed too strongly. It is so important that one should consider any child as at least potentially tuberculous if not actually infected who has for any length of time been exposed to an active case of tuberculosis in the home. A Norwegian city, said to be ridden with tuberculosis, has decreased its child mortality from tuberculosis by 50 per cent by an obligatory declaration and isolation of all children of tuberculous parents from birth to three years of age.

The hereditary factor in tuberculosis has long been a subject of much discussion. For years it was believed to be an inherited disease. This we now know is not true. There are a few authentic cases on record where a child has been born with advanced tuberculosis. Children are also occasionally born with other infectious diseases, namely, the exanthemata. This is easily explained by the mother having the specific organism in her blood stream and its gaining entrance to the fetal circulation through the placenta. It is inconceivable that the tubercle bacillus could be transmitted to the offspring through either the sperm-cell or through the ovum. It is quite possible, however, that the child of a tuberculous parent may be born with a "tuberculous diathesis," that is, with a predisposition toward the disease. Govarerts speaks of this inherited diathesis as follows: "Tuberculosis is not an inheritable character in the sense in which eye color is inheritable. It belongs to a second kind of heredity called 'indirect heredity.' Infection and immunity are causes, but they do not exclude inheritance. Biologically speaking, people inherit directly a constitutional make-up, possibly functional, chemical, and structural with a certain amount of power to resist tuberculosis and other related diseases." Such a statement is not contradictory to a previous reference to the hereditary factor in tuberculosis; a child born of parents who are arrested cases of tuberculosis would, according to the laws of immunity, have a greater natural immunity to tuberculosis than a child whose parents have never had a tuberculous infection. On the other hand, a child born of parents suffering from advanced active tuberculosis would have little or no immunity not only for tuberculosis but other infectious diseases.

MODES OF INVASION

There are three modes of invasion, one through the respiratory tract, another through the gastro-intestinal tract and a third through the skin. The mouth and upper respiratory tract undoubtedly form the chief portal of entry as evidenced by the high percentage of children showing an involvement of the cervical lymph glands. The young child puts everything into his mouth. He crawls about the floor or plays in the street where the fresh sputum of a thoughtless adult may be found. Healthy mucous membrane is impermeable but it becomes permeable when diseased, as in catarrh or during a tonsillar infection. This permits the tubercle bacillus, when present in the air, in food or on the child's hands, to pass through the membrane and be taken up by the regional lymph glands, which in this case are the cervical glands. The organism may be inhaled into the lungs and thus gain entrance to the bronchial glands at the hilus. When swallowed the bacillus is not destroyed by the gastric juice in the stomach but passes on into the intestine, through which it gains access to the mesenteric lymph

glands. This explains why bovine infection is so common in cervical and mesentery gland involvement and rare in bronchial gland tuberculosis. The same reasoning strongly opposes the view that the infection passes down the cervical chain to the bronchial glands and then to the lungs.

Rarely the skin becomes the portal of entry. When this is so, it is through an abrasion. The ease with which the tender mucous membrane of the nose is injured by the child picking his nose accounts for the frequency of lupus vulgaris having its origin in this location.

SYMPTOMATOLOGY AND DIAGNOSIS

Just as in the adult, the child may have tuberculosis involving any organ or group of organs. In the child certain forms of tuberculosis are the rule, so when the parenchyma of a child's lungs or a kidney becomes infected we no longer say that the child has "juvenile tuberculosis" but that he has an adult type of infection. The adult type of infection in a child differs so little from that in an adult that it hardly requires particular mention here.

In juvenile tuberculosis the lymph glands are perhaps most frequently the site of involvement. Tuberculous glands *per se* do not cause death. For this reason death rate is not a true criterion as to the prevalence of the disease. Tuberculous glands on the contrary tend to produce an immunity to the disease which protects the child in later life. We rarely see adults suffering from advanced tuberculosis who as children have had glandular involvement. The same is also true of lupus vulgaris and of tuberculosis of bones and joints.

If the glands involved happen to be the cervical glands and the involvement is sufficient, there is no great difficulty in differentiating them from other conditions and making a correct diagnosis. But, if the involvement be slight or should it be the bronchial or mesenteric glands that are involved instead, an early correct diagnosis may be very difficult to make. In fact, early diagnosis is not only often obscure but definite clinical signs and symptoms are frequently entirely wanting. In these cases one must be guided largely by the history and exclusion of other probable causes. In the history, exposure in the home is almost diagnostic. Failure to gain weight over a period of six months is fully as significant as actual loss of weight. One must inquire carefully as to the child's diet, eating of candy between meals, hours of rest, whether or not there is proper ventilation in the sleeping room and as to the number of hours spent out-of-doors in the sunshine. Frequently cases thought at first to be tuberculosis prove to be suffering from malnutrition and improper home care.

It is impossible, as in many diseases, to draw a picture of a so-called "classical" or "typical" case, for there is no one symptom or group of symp-

toms which may be said to be pathognomonic of early glandular tuberculosis. In making the diagnosis, the history, the appearance of the child and the physical examination must all be taken into consideration. Not uncommonly he appears ill, has a sallow complexion and a tired expression. The cheeks may be slightly flushed. He is not infrequently underweight and poorly developed for his age. His posture is poor, particularly when sitting. The chest is flat, the hands are cold and moist. The child has no ambition, tires easily and does not care to play with other children. The eyes are bright and the lashes are long and curl upward; there is the more or less characteristic pouty upper lip. Hypertrichosis is generally present—at the nape and upper arms. Distended or broken superficial capillaries across the shoulder-girdle are not infrequently met with. The onset is, of course, insidious.

In making the diagnosis of bronchial gland tuberculosis Hawes [1] requires the following criteria. He insists on the first and believes also in the great majority of cases that there should be x-ray evidence of lymph-node enlargement. The other three points are important but not essential to the diagnosis.

1. A positive skin tuberculin test unless the child has recently recovered from measles or any of the other acute infections which might lead to a negative test, or unless the child has advanced tuberculosis.

2. A definite history of exposure either to human or bovine sources of tuberculosis.

3. Constitutional signs and symptoms, particularly loss of weight or failure to gain weight, along with "ease of tire" or fever or rapid pulse.

4. The presence of enlarged bronchial nodes as shown by x-ray or by clinical examination of the chest.

5. The absence of other evident sources of infection or toxemia, such as: (*a*) infected tonsils or adenoids; (*b*) carious teeth; (*c*) intestinal disturbances, particularly chronic appendicitis, and (*d*) other probable sources of infection, such as middle ear, lymph-nodes, bronchopneumonia, measles, whooping-cough, etc.

The local objective findings in bronchial node tuberculosis are extremely variable. In a child the normal variations in breath sounds are so great that little significance can be attached to them. If intrascapular dulness be found it is of value, but again this is a difficult sign to elicit with any degree of certainty. There has been much dispute regarding the value of D'Espine's sign. It is found to be present in a certain percentage of children who upon

[1] John B. Hawes, 2nd, "Juvenile Tuberculosis," *Am. Rev. Tuberc.,* September, 1922.

x-ray examination show no apparent enlargement of the bronchial glands. A negative D'Espine sign is of considerable value in excluding bronchial node enlargement. Chadwick places considerable emphasis on the fixation of the skin between the scapulæ. He has also found a certain firmness of pressure over the apex on the side of greater involvement. A few fine, dry crackling râles are found at times between the scapulæ and also along the border of the manubrium sterni.

X-ray aids greatly in confirming the diagnosis in these cases. Repeated x-ray pictures are an index of the prognosis as they show definitely how the course is progressing. In the early x-ray pictures of these cases the hilus nodes appear as soft fluffy shadows somewhat resembling a ball of cotton. These usually vary in size from $\frac{1}{4}$ to 2 centimeters in diameter. X-ray pictures taken six months later may be interposed on the first pictures, showing the changes in identical glands. In the case of healing, the nodes lose their fluffy appearance and assume a definite hard outline owing to calcification having taken place. On the other hand, if the case has progressed unfavorably, the nodes appear larger, fluffier and are increased in number. No evidence of parenchymal involvement is found in these cases, thus indicating that the lung tissue itself is not diseased.

CERVICAL GLANDS

Fifty to 75 per cent of all children have palpable cervical glands. Many conditions other than tuberculosis produce glandular enlargement in this region.

Nevertheless, the cervical glands are those most commonly primarily involved in tuberculous adenitis. The reason for this, as has previously been stated, is that the upper respiratory and upper intestinal tracts form the chief portals of entry of the tubercle bacillus. As these two tracts in this region are drained through the same lymph channels we naturally find these cervical glands frequently involved. Bacilli cannot permeate normal mucous membrane, therefore, in order for organisms to gain entrance the membrane must be diseased. Simple colds and chronic catarrhal conditions are the most common causes which make invasion possible, thus it is very important to keep the child free from colds which predispose him to serious infection. Here again the diagnosis, except where the involvement is great, must often be made by the elimination of other frequent causes of enlarged cervical glands, chief among which are diseased tonsils and adenoids, carious teeth, stomatitis, eczema, pediculosis, lymphosarcoma, Hodgkin's disease, and lymphatic anemia. In the majority of these conditions the primary factor in the glandular enlargement is so evident that little need be said regarding their differentiation. The blood-picture is at times of value. This is par-

ticularly true in lymphatic anemia. When there is any doubt a biopsy is always conclusive.

In early cases of tuberculous cervical adenitis the glands are not visible but may be felt upon palpation as discrete shotlike nodules; those most frequently involved being in the lower posterior cervical chains. Later they spread to include the anterior glands in both the upper and lower cervical regions. Not infrequently on deep palpation glands may be found buried below the clavicles. When advanced they are no longer discrete but confluent, and vary from the size of a pea to that of a large hen's egg. They are soft and freely movable. Still later on they break down and suppurate. Only rarely do we now see far advanced suppurating cases of cervical gland tuberculosis. The reason for this is twofold: first, removal of the bovine sources of infection; second, diagnosis is made earlier and the proper treatment instituted before the infection has progressed to this extent.

In addition to the local findings the child shows general evidence of malnutrition and other constitutional symptoms similar to those described under bronchial node involvement.

The bovine type of bacillus is found to be the etiological factor in a large percentage of these cases as indicated by the decrease in the number of cases found in cities having a rigid supervision of the milk supply. As bronchial gland tuberculosis is usually caused by the human type of bacillus, it would seem probable that bronchial gland infection is not caused by a downward extension of the infection from the cervical nodes. This would be in accord with the embryological development of these respective glands.

PRIMARY MESENTERIC NODE TUBERCULOSIS

Obviously this condition is of bovine origin. The diagnosis of primary tuberculosis of the mesenteric glands is naturally difficult to make. Here again the diagnosis is made more by the exclusion of other likely causes. Local examination as a rule reveals nothing. Consequently the diagnosis rests upon the history, a positive tuberculin reaction and the general constitutional symptoms. The history and general constitutional symptoms are the same as those that have previously been described under bronchial node involvement. The latter are erroneously attributed to dietary indiscretions. Constipation or at times moderate diarrhea may be found. Not infrequently the condition is unsuspected and revealed only at necropsy, the patient having died from some intercurrent infection. There has been much divergence of opinion as to whether or not extension of mesenteric gland tuberculosis may cause bronchial node involvement. The more recent view is that it does not. This belief is based largely on the etiological factors involved in these two conditions.

Quite naturally in general miliary tuberculosis we find extensive involvement of the mesenteric glands. This is to be expected, and does not need to be taken into consideration in the discussion of primary abdominal node tuberculosis.

The chief conditions from which primary mesenteric gland tuberculosis need to be differentiated are malnutrition, chronic appendicitis, lymphosarcoma, lymphatic anemia, and Hodgkin's disease. Since the last three are rare and usually exhibit a general lymphadenitis, they are not particularly difficult to differentiate. In infancy and early childhood the tuberculin test is of greatest value in distinguishing this condition from cases of malnutrition. In chronic appendicitis there is often a history of repeated acute attacks, the abdominal examination usually revealing right-sided muscle rigidity, tenderness in the right lower quadrant and not infrequently muscle spasm upon deep palpation over the region of the appendix.

However, outside of the involvement of glands, bones and joints and skin, tuberculous infections are comparatively rare before adult life, aside from miliary tuberculosis. They do occur, though, so that it is necessary to keep them in mind when examining a child for any cause whatsoever. Most deaths from tuberculosis during infancy and childhood are caused by generalized infection or miliary tuberculosis. This in a large majority of cases terminates in tuberculous meningitis.

LUPUS VULGARIS

Formerly this condition was attributed to the bovine type of infection, but more recent investigations have proved that the human type is responsible for nearly 90 per cent of the cases. A child many infect himself through an abrasion of the skin by means of dirty hands contaminated with tubercle bacilli, or by the inhalation of the organisms which later may gain entrance through an abrasion of the nasal mucosa. A large percentage of the cases have their origin about the nose. It is essentially a disease of the poor, associated with defective hygiene.

In the nose the septum, floor, and inferior turbinates are the most frequent parts involved. The early lesion consists of large pale moist granulations which first appear in crops. These later become dry and crusted, the crusts falling off and leaving an eroded surface. Still later, if the infection is permitted to progress, the cartilage becomes affected, resulting in the well-known deformity. Spreading directly from the nose the surrounding skin not infrequently becomes involved, and by auto-infection is often carried to other parts of the body. There is a great tendency towards chronicity. When the skin finally heals an ugly cicatrix remains not infrequently with keloid formation.

CENTRAL NERVOUS SYSTEM

Meningitis.—Tuberculous meningitis is always secondary to tuberculosis in another portion of the body; the lungs or lymph-nodes being the seats of the primary lesion in the great majority of instances. It may be defined as a subacute or acute inflammation of the arachnoid and pia mater of the brain and spinal cord. The causative agent is the tubercle bacillus which may reach the meninges by way of the blood stream as in a generalized miliary tuberculosis, by way of the basilar lymph-vessels, or by direct extension from a tuberculous process such as an otitis media.

The disease is very common in children and shows a remarkable predilection for infants. Cases have been reported under three months of age but the greatest mortality period has been determined as from twelve to twenty-four months of age. During the first and third years there is also a high incidence. This form of tuberculosis is found all through infancy, childhood, and adolescence in an alarming number of instances.

Sex does not play an important part in the disease. The consensus of opinion is that males are more frequently attacked but only to a very slight degree greater than females. Previous illnesses play an important rôle as predisposing agents. Measles, whooping-cough, pneumonia, influenza, otitis media, tonsillitis, tonsillectomy and bronchitis have been reported as preceding tuberculous meningitis in a sufficient number of instances to establish a definite relationship with the condition. When coupled with poor hygienic conditions, *e.g.*, living in close and prolonged contact with careless tuberculous patients, especially in dark, damp and ill ventilated houses, or living or sleeping in places which have become contaminated with germs from sick people who were careless in spitting, these infections favor the onset of the disease by lowering the resistance of the child.

In the vast majority of cases tuberculous meningitis is caused by the human type of bacillus. Bovine infection is still a definite cause and is most frequent in those localities which do not require pasteurization of milk. By 1924 modern dairying methods had reduced the incidence of bovine type of meningitis in New York City to less than 2 per cent. Similar results have been obtained in other communities where milk is pasteurized.

Trauma seems to bear a definite bearing on the development of tuberculous meningitis. Blows on the head or spine, operations on tuberculous joints or the fixation procedures employed in dealing with Pott's disease are often the initiating factors in tuberculous meningitis. A great majority of the cases occur in the spring of the year.

The lesions may be faint or well marked. In typical cases there is a massive localization of the exudate at the base of the brain and along the superior work of the cerebellum. This exudate is a purulent, yellow, cheesy

mass that may reach an inch in thickness. There is an accompanying hyperemia of the brain with the finding of miliary tubercles along the olfactory tract, the fissure of Sylvius, and on the inferior surface of the frontal lobe. In many instances the meninges alone are not involved but the process goes deeper and involves the tissue of the brain, giving rise to a meningo-encephalitis. The engorgement causes increased intracranial pressure, resulting in the flattening of the convolutions and the obliteration of the sulci. The hyperemia and increased intracranial pressure bring about an acute hydrocephalus in some instances. The spinal cord may or may not be involved.

The onset is usually insidious, the initial symptoms sometimes being masked by the original disease—whooping-cough, influenza, etc. In many cases, however, the prodromata are well marked, the most common being irritability, anorexia, emaciation, mental dullness, insomnia, paroxysmal headache and a slight temperature. An important trio of symptoms has for many years been observed at the onset of this condition: *i.e.*, headache, vertigo on change of position, and vomiting without relation to the taking of food. Meningeal irritation gives rise to sensory, motor and psychic symptoms.

Symptoms.—Sensory.—The patient complains of pains in the chest and abdomen. Suboccipital headache is pronounced. There is an early development of apathy, dullness and somnolence.

Motor.—There are facial twitchings, grinding of the teeth, trismus, and a rapid change in the tonicity of the muscles. A muscle may be absolutely rigid and an hour later relaxed. Spasm of the facial muscles is very common. A true Jacksonian convulsion may occur. Retraction of the neck is present but not to such a marked degree as is found in other forms of meningitis. The head is frequently rolled from side to side in a restless fashion. In young children there is a tendency to assume the fetal position. Strabismus is always present, the eyes usually being deviated to the outer side. Third nerve paralysis is common. Ophthalmoplegia and nystagmus are frequently observed. Paralysis of the extremities is rare.

Psychic.—The psychic symptoms are of long duration. Somnolence is very pronounced. The mind wanders. There may be delirium similar to that encountered in delirium tremens. Later there is coma. Hydrocephalus develops rapidly and is associated with the "hydrocephalic cry," a peculiar, sharp, piercing cry given by the patient while asleep.

Optic neuritis and choked disk may occur. Choroid tubercles occur but are not easy to recognize.

Other symptoms are in the main quite similar to those encountered in epidemic cerebrospinal meningitis but are usually less intense. Emaciation occurs rapidly and is probably due to the anorexia, trophic disturbances and fever. Herpes labialis occurs. Taches cérébrales may be demonstrated but

are of no clinical significance. At first the pupils are contracted and active to light but in the later stages they become dilated, unequal, and reactionless. In the early stages the tendon reflexes are usually increased with demonstrable ankle-clonus and Babinski phenomenon. The cutaneous reflexes are also increased in the early stages. A dissociation of the pulse and temperature is more common than in any other form of meningitis. The pulse is slow and irregular until towards the close, when it becomes more rapid. The temperature is usually high, 103°-105°. Obstinate constipation with retention of urine is the rule. Monoplegia and hemiplegia are occasionally met with. Motor aphasia and epileptic seizures are quite common.

The cerebrospinal fluid is under increased tension. It is characteristically clear and colorless but it may be erythrochromic and rarely it is opalescent. A well marked lymphocytosis (95 per cent) is generally seen on microscopic examination. The fluid never clots but on standing a delicate web forms in the fluid. Tubercle bacilli may be demonstrated in the spinal fluid in every case of tuberculous meningitis. A differential point is the failure of the spinal fluid of tuberculous meningitis to reduce Fehling's solution.

Diagnosis.—There is a wide deviation in the symptoms as they depend upon the nature, location and multiplicity of the lesions. The stage of invasion is usually of several weeks' duration. During it we have loss of weight, irritability, restlessness, headache, constipation and a slight temperature. This stage gradually passes into the stage of inflammation where the fever is increased, the headache becomes more severe, and there is also photophobia and hyperacusis. The patient is usually in a semisomnolent condition, arousing only to answer questions when spoken to. The pulse is slow, but becomes quickened by exertion or excitement. Alternate pallor and flushing are not uncommon vasomotor reactions. At this time there appears a rigidity of the muscles of the neck and back, often with retraction of the head, grinding of the teeth and pulling up of the corners of the mouth. Early the pupils are contracted, later they become dilated, associated with moderately choked disks. Miliary tubercles of the choroid are seen at times. Convulsions are usually light. The reflexes are at first increased, later there being a positive Kernig, Babinski and Gordon. The patient gradually becomes unconscious. The pupils are dilated and the eyes rolled up and out— the lids open in "coma vigil." The back and neck are spastic while the extremities are relaxed. The pulse becomes rapid, the respiration irregular and the temperature falls; not infrequently there is retention of urine toward the end. Death may follow a convulsion or come on gradually, the patient first becoming cold and cyanotic.

Long prodromata, with moderate temperature, bradycardia and constipation, are always suggestive of tuberculosis. Other forms of meningitis begin acutely with a high initial fever and run a rapid course. A focus of

infection either active or latent is always suggestive. However, the bacilli must be found in the spinal fluid in order definitely to confirm the diagnosis.

Prognosis and Course.—The prognosis is generally hopeless; a few cases of tuberculous meningitis have been reported as recovered but in the vast majority of instances the patient dies. Rarely the disease is fatal in a few days but generally death occurs in from four to six weeks. The disease may become chronic and last for months.

Treatment.—Repeated lumbar puncture relieves many of the symptoms. Sedatives, such as the bromids and codein, should be used to control restlessness and pain. Tuberculin has been used in small doses in protracted cases.

Brain Tumors.—Fifty per cent of the brain tumors in children under fifteen years of age are tuberculomata. One case is reported in the literature occurring in an infant only twenty-three days old. Brain tumors may be either single or multiple and vary in size from that of a split pea to a hen's egg. Meningitis may result from direct extension involving the meninges.

Tuberculomata run a chronic course. The symptoms do not differ materially from those produced by other forms of tumors. Symptoms may be entirely wanting, particularly when the lesion is located in the silent area. Headache, optic neuritis, and vomiting, however, are fairly constant symptoms associated with tuberculoma.

At times tuberculous tumors are found in the cord. These may be either single or multiple, the symptoms naturally depending upon the location.

In cases where the lesion is thought to be single and localizing symptoms are sufficient, operative treatment is indicated.

EYES

Tuberculous infection of the eye and the accessory structures are among the rare forms of tuberculosis found in children. At times they occur without other apparent evidences of tuberculosis and without impairment of health. If the lesion be slight, resolution may take place without producing great damage.

Among the superficial lesions are lupus of the eyelids, granulations or ulcers of the conjunctiva and tuberculosis involving the lacrimal sac. Destruction of the lid may result from lupus leaving the cornea exposed and liable to injury. The cornea and deeper structure may themselves become involved, owing to the proximity to a lesion involving the eyelid. Tuberculous granulations and ulcers of the conjunctiva are difficult to distinguish from similar conditions of different etiology. Their diagnosis and treatment belong to the ophthalmologist. Tuberculous involvement of the lacrimal sac is not an uncommon condition; a considerable number of such cases

have been reported. The condition is caused by direct extension from a nasal involvement or by downward extension from an infection of the conjunctival sac. In cases where the nose is the site of the primary lesion the conjunctival sac not infrequently becomes infected secondarily to lacrimal sac involvement and vice versa. When the primary source is not evident the differentiation of tuberculous dacryocystitis from other forms is a problem for the ophthalmologist.

Tuberculosis involving the deeper structures of the eye, particularly in children, is a condition of such rarity that its discussion is not warranted here. It may be found in a textbook on eye diseases.

EAR

Tuberculosis as a disease of the ear was described long before the discovery of the tubercle bacillus. It is not an uncommon condition in children. The disease appears first as an involvement of the middle ear; later the internal ear becomes involved. The external ear invariably escapes except as it is secondarily involved by the discharge through the auditory canal. By extension the temporal bone is not infrequently infected, and in the same way the facial nerve is often affected.

The organisms gain entrance to the middle ear through the eustachian tube. Hypertrophied tonsils and adenoids, even though not themselves tuberculous, are factors of extreme importance predisposing to this condition.

Tuberculous involvement of the middle ear, particularly in children, is undoubtedly more frequent than statistics would indicate. This is because of the exceeding difficulty of obtaining the tubercle bacilli from the discharge. Early smears made from this secretion as a rule reveal the tubercle bacilli; later the staphylococcus or streptococcus are invariably found as secondary invaders. Guinea-pig inoculations made from the early discharge often demonstrate the true nature of the infection.

The most striking clinical feature in tuberculous otitis media is the lack of pain which is so frequently the outstanding symptom in other infections of the middle ear. Infections of tuberculous origin tend toward great chronicity. There is an early serous discharge which is very irritating to the surrounding tissue and not infrequently causes an exceedingly obstinate eczema. The regional lymph glands are usually enlarged and also painless. Later in the course the discharge becomes purulent. This change is due to secondary infection, usually the staphylococcus or the streptococcus.

This condition is one which is often refractory to treatment. The local treatment belongs to the otologist. From the prophylactic standpoint removal of hypertrophied tonsils and adenoids in children is important. This

markedly reduces the tendency towards middle ear infection. Of equal importance with the local treatment in these chronic cases is the building up of the child's general health by dietary and hygienic measures.

RESPIRATORY SYSTEM

Nasal.—Nasal tuberculomata are at times found. These appear as smooth, pale red tumors either on or suspended from the mucosa. Treatment is by snaring and cautery.

Tuberculous Ulcers.—This is a rare condition. When found they are generally located in the posterior portion of the nares. They are usually due to secondary infection from an open pulmonary lesion and do not differ materially from the lesions on the nasal mucosa already described under lupus vulgaris. Treatment is to scrape and cauterize.

Pharynx.—The pharynx is rarely if ever primarily involved. Involvement occurs most frequently in cases of miliary tuberculosis. The lesions appear as small discrete white spots on a pink background. These later pass on to ulceration. The true nature of the lesions is usually not determined unless microscopic examination is made.

Laryngeal Tuberculosis.—This is a rare condition in children under twelve. It may be said to occur only secondarily to an active pulmonary lesion or in the case of miliary tuberculosis by means of a blood stream infection. As pulmonary tuberculosis in children runs an exceedingly rapid course there is not sufficient time for a laryngeal complication to arise.

Tonsils and Adenoids.—Tuberculosis of tonsils and adenoids is not met with as frequently as one might expect. Of all tonsils removed only about 6 per cent show evidence of tuberculous infection. The organism is usually bovine in type. Infection of this tissue bears the same relation to juvenile tuberculosis as does tuberculosis of the cervical glands. Thus, when tuberculosis is found in tonsillar tissue one should not become unduly alarmed. There is apparently no connection between pulmonary tuberculosis and tuberculosis of tonsils and adenoids. No larger percentage of children in whom tuberculosis of the tonsils has been found develop pulmonary tuberculosis later in life than children who have not had tuberculous tonsils. It is impossible to recognize tuberculosis of tonsils or adenoids in the gross unless there is superficial ulceration. The diagnosis must be made microscopically.

Pulmonary Tuberculosis in Childhood.—This is not a common condition. When it does occur both the subjective and objective symptoms are similar to those found in adult pulmonary tuberculosis. Their clinical characteristics are so well known that one does not need to enumerate them here. In infancy and childhood pulmonary involvement is usually associated

with miliary tuberculosis. Occasionally we see cases of pulmonary tuberculosis in children which are apparently caused by direct extension from involvement of the bronchial nodes. The prognosis of pulmonary tuberculosis in infancy and childhood is always grave. It invariably runs a short and rapid course, not infrequently terminating in meningitis. By persistent searching, tubercle bacilli are found in the sputum in the majority of these cases, but obtaining sputum from an infant is a difficult procedure. Holt suggests irritating the pharyngeal mucosa with a cotton swab on an applicator, thus causing the child to cough. The spray containing the organisms is caught on the swab from which smears can be made.

Measles and whooping-cough play an extremely important rôle in predisposing the child to pulmonary tuberculosis. Many theories have been advanced but no really satisfactory explanation has ever been given to account for this. Only too frequently do we see active pulmonary cases of tuberculosis following in the wake of these two infectious diseases. Not uncommonly mothers state that their children have never been free from cough since they had measles or whooping-cough. On examination of such children not infrequently definite evidence of an active pulmonary tuberculosis is found.

There are several conditions which in some cases might give slight difficulty in differentiating. Among these are the following:

Chronic Bronchitis.—This disease often follows measles and whooping-cough, giving similar subjective symptoms to pulmonary tuberculosis. Examination of the sputum and x-ray should obviate any difficulty in distinguishing between these two conditions.

Asthma.—Asthma should not be difficult to differentiate. Here one finds the typical asthmatic wheezes, at least during an acute exacerbation. X-ray is also of value.

Bronchiectasis.—The sputum in this condition is negative for tubercle bacilli. There is not the impairment in health that one would expect where the objective findings are due to tuberculosis. Again the x-ray is of value.

Bronchopneumonia.—This condition should really cause but little difficulty in differentiating as there is usually a history of an acute onset. The sputum is negative for tubercle bacilli, the pneumococcus usually being the predominating organism. A leukocyte count under 10,000 favors tuberculosis, although a count over 20,000 by no means excludes that disease. X-ray is of value.

Pulmonary Abscess.—This is usually secondary to lobar pneumonia. The type of sputum is characteristic as is also the odor. Recently a spirochæta has been isolated in these cases which may prove of further diagnostic aid. The x-ray is particularly valuable in these cases.

Unresolved Lobar Pneumonia.—This condition should cause no difficulty in distinguishing from pulmonary tuberculosis as the history is often a guide to the nature of the existing lesion. Sputum examination and x-ray are valuable adjuncts.

Pleurisy.—Pleurisy is a rare condition in children. In infancy and childhood it does not bear the same relation to tuberculosis that it does in adult life. In children it is usually a complication of pneumonia. When tuberculous pleurisy does occur the prognosis is good, fibrous changes continuing for many years. They frequently regress and cause complete disappearance of the disease.

Tuberculous Pericarditis.—This condition occurs only rarely and is usually a complication of miliary tuberculosis. It does not differ clinically from other forms of pericarditis and is distinguished only by microscopic examination.

GASTRO-INTESTINAL SYSTEM

Tuberculous infections of the gastro-intestinal system are invariably bovine in type. We rarely find tuberculous lesions in the intestinal tract in children under one year of age. The maximum incidence is found in children during the third year of life. Any portion of the gastro-intestinal tract may be the seat of tuberculous involvement. The intestinal mucosa must, however, be itself previously diseased in order to become infected by the tubercle bacillus. We know that this organism is not killed by gastric juice in ninety minutes, which means that virulent bacilli are carried on into the intestine. Although we not infrequently find tuberculosis involving the mesenteric lymph-nodes, we but rarely find tuberculosis which is apparently primary in the intestine. Tuberculous enteritis and peritonitis are frequently indicative of a generalized tuberculosis.

Stomach.—Tuberculous ulcers are found involving the gastric mucosa. They are, however, never found apart from tuberculous enteritis. They are recognized only postmortem.

Appendicitis.—Tuberculosis is not an infrequent cause of appendicitis in children and does not differ clinically from other forms of the disease. There is no way in which to distinguish it except postoperatively and then, as a rule, pathological examination is necessary. Appendicitis of a tuberculous nature apparently bears the same relation to other forms of tuberculosis as does tuberculosis of the tonsils.

Enteritis.—Tuberculous enteritis *per se* is said by some never to exist, being always associated with the glandular involvement and peritonitis. The most prominent symptom attributable to enteritis is diarrhea. However, early in the course, constipation is often met with, while later diarrhea and constipation may at times alternate. The amount of diarrhea is directly

proportionate to the extent of the involvement of the intestinal mucosa. Emaciation naturally soon becomes a prominent symptom if the diarrhea persists for any length of time and unless the condition becomes arrested the patient soon dies from exhaustion. Occasionally perforation takes place, causing death within a few hours.

Peritonitis.—There are two forms of peritonitis, the ascitic and the plastic form. When associated with miliary tuberculosis it usually occurs in the preterminal stages and is a grave omen. When peritonitis occurs *per se* the prognosis in many cases is not as grave as has previously been thought. In these cases it naturally depends upon the early recognition of the condition, the severity, and the promptness with which proper treatment is instituted.

Ascitic Form.—In this form the onset as a rule is acute. Early there is a pyrexia of a few days' duration which precedes a generalized pain in the abdomen, which becomes rapidly distended with fluid. If left untreated the fluid may be slowly absorbed over a period varying from a few weeks to several months. In these cases symptoms characteristic of the plastic form not infrequently slowly supervene. Following paracentesis the fever quickly subsides and in some cases resolution takes place unaccompanied by other complications. Repeated paracentesis may be necessary, which of course at times is without avail. The fluid is an exudate from which even when centrifuged it is difficult to obtain smears showing the organisms. Guinea-pig inoculations, however, usually prove the presence of the tubercle bacilli.

Plastic Form.—Some believe that the plastic form does not occur without involvement of the abdominal glands and intestine as well as the peritoneum. Symptoms attributable to the associated enteritis are easily discernible. The onset in this form is insidious with vague indefinite symptoms. The physician is usually consulted because the child looks pasty, has no appetite, and does not gain weight.

Diarrhea or constipation associated with colicky pains are early valuable signs. The abdomen is usually distended. On palpation there are areas of tenderness and if the distention is not too great an enlargement of the spleen may be felt. Later the abdomen is protuberant, giving a tympanitic note upon percussion. The skin over the abdomen is thin, dry and inelastic, through which the superficial veins appear prominently. Masses, due to matted omentum forming bands in which are caught loops of intestine, are frequently palpated, usually low down in the abdomen. This condition often leads to intestinal obstruction, the true etiology of which is sometimes not ascertained until operation. The temperature varies greatly, being seldom high and frequently normal. Vomiting is rarely of grave severity and

when it occurs is usually an early symptom. Diarrhea and constipation are very variable. Constipation most frequently occurs early in the course, while diarrhea appears as a later manifestation. At times diarrhea and constipation may alternate. The prognosis depends upon the amount of associated intestinal involvement, the extent of which is usually directly proportional to the diarrhea. Occasionally perforation of the intestine takes place, indicated by excruciating pain and tenderness with manifestations of shock. In these cases prompt surgical intervention is necessary in order to save the patient.

Other conditions found in adults with which tuberculous peritonitis might be confused are rarely met with in childhood.

Cirrhosis of the Liver.—This is an extremely rare condition in childhood. When it does occur it is usually associated with congenital syphilis which produces so many other signs and symptoms that there should be no difficulty in differentiating it.

Thrombosis of the Portal Vein.—This also is a rare condition in childhood which usually follows a septic condition, the history of which should leave no doubt in the examiner's mind.

Typhoid Fever.—In some cases, if rose spots were not found, this might be confusing from the clinical aspect. But laboratory measures, such as a positive Widal test, blood cultures, stool and urine examinations, and a low leukocyte count, should leave no question as to the presence of this condition.

Malaria.—In this disease the abdomen is not protuberant, there is a cycle of fever and chills and the characteristic blood-picture.

Rickets.—Although the abdomen is prominent in rickets there is no pain or diarrhea. In this disease also there are enlarged epiphyses, the bowing, the rosary, shape of the head, head sweating, patent fontanel, any one of which would be indicative of the condition and finally the x-ray would help differentiate this disease.

Chronic Appendicitis.—Lack of distention, history of acute attacks and symptoms pointing usually to the right lower quadrant should aid one to distinguish between these two conditions.

TUBERCULOSIS OF OTHER ABDOMINAL VISCERA

Liver.—This is probably never primarily involved in tuberculosis, being always associated with a miliary condition. Tuberculosis causes fibrous thickening, producing a hypertrophic cirrhosis. There may be an accompanying jaundice and an associated ascites. Not infrequently the liver becomes involved so late in the disease that these two last-mentioned complications do not have sufficient time in which to occur.

Spleen.—Changes in the spleen occur only in miliary tuberculosis and are the changes of secondary anemia. The capsule is thickened and the organ enlarged.

Adrenals.—These are rarely involved and only in the later stages of miliary tuberculosis. Clinical evidence suggesting foci in the adrenals is rarely seen, its presence being noted only on microscopic examination. Once in a while there is a bronzing of the skin shortly before death in miliary tuberculosis which may be attributed to disease of these organs.

GENITO-URINARY SYSTEM

Kidneys.—The kidneys are seldom if ever the primary site of infection. In children kidney complications are rarely met except in miliary tuberculosis. When the condition does occur its symptoms and diagnosis do not differ from those in the adult.

Genital organs and genitalia tuberculosis of the uterus and appendages is a rare condition in children and seldom exists except in generalized tuberculosis. The same may be said of tuberculosis of the testicles and epididymis during childhood. Tuberculoma and tuberculous ulcers of the vulva, usually produced by auto-infection, may occur during childhood, but are extremely rare.

PSYCHIC DISTURBANCES

It is very difficult to say just what part tuberculous infection in childhood plays in predisposing the individual to later mental disorders, particularly dementia præcox, epileptic and hysterical convulsions. There are so many other factors, such as family predisposition and environment, which enter into the background in mental disorders and play such an enormous rôle that one can hardly say that tuberculosis is more than a contributing factor in an already predisposed individual. There is, however, in any debilitating disease; a mental factor which must be taken into consideration. The exhaustion psychoses which are met with in adults following debilitating conditions are rarely seen in children. The malnourished child is always irritable and restless, does not play normally with other children and in this way produces a problem in child psychology. This is no more true in tuberculosis than in other diseases which may cause an impairment in health for a considerable period of time.

MILIARY TUBERCULOSIS

This condition not infrequently occurs during infancy and childhood. It represents the minimum of resistance to tuberculous infection. The symp-

toms and clinical picture vary, depending upon the organ or groups of organs chiefly involved. Where there is general involvement or a rapidly progressing infection the prognosis is unfavorable, the majority of cases terminating in meningitis. Kelynack has described four types—the marasmic type, the acute febrile type, the meningeal type, and the pulmonary type.

Marasmic Type.—The symptoms are those of a progressive emaciation with gastro-intestinal disturbances. Pulmonary symptoms in such a case may be entirely absent. The pulse is rapid and small and the temperature not marked, being sometimes subnormal. The spleen frequently is enlarged.

Acute Febrile Type.—This condition very closely resembles the marasmic type with the exception that there is a marked fever which may be continuous or remittent. Associated with this is a rapidly increasing dyspnea, cyanosis and exhaustion.

Meningeal Type.—This is perhaps the most characteristic form. The symptoms of meningeal irritation may occur as the first evidence of involvement. However, meningeal symptoms more frequently occur as a terminating factor in generalized tuberculous infection.

Pulmonary Type.—This type may begin acutely, closely resembling a severe bronchopneumonia or the onset may be insidious with anorexia, languor and debility. The cough is severe and is not as a rule accompanied by expectoration. The lungs are studded with minute tubercles which may be so close together as to give almost complete consolidation.

BONES AND JOINTS

Tuberculosis involving bones and joints occurs more commonly in children than in adults, and most frequently between the ages of five and fifteen. Males are said to be more often affected than females. Although tuberculosis of bones and joints is probably never primary, the condition, nevertheless, is essentially a local disease. Trauma is thought by some to be a predisposing factor. The spine, hip and knee, in the order named, are the parts most frequently affected, while involvement of the ankle, elbow and other joints occurs with about the same frequency. In the long bones the process begins in the epiphyseal end and in the marrow and then spreads to the bony trabeculæ. Rarely does the process begin in the compact cortical area and is said never to begin in cartilage. Of the long bones the ribs are most commonly affected. Most authorities agree that tuberculosis of joints is caused by an extension of a lesion through the synovial membrane from the disease in an adjoining bone.

The earliest bone lesion is the tubercle, the pathogenesis of which is essentially the same as in other tissue. The tubercle increases in size, caseation takes place, later going on to abscess formation. Necrosis of bone occurs,

leaving a sequestrum in the center. It is these sequestra which are expelled through sinuses. Associated with the breaking down of tuberculous tissue is abscess formation of a peculiar nature known as "cold abscess," which has none of the ordinary characteristics. "Cold abscesses" may be very misleading. Not infrequently they have their origin in the cervical or upper thoracic region points in the femoral triangle or psoas region. No attempt should be made to drain a cold abscess. The condition is treated by building up the patient's general health.

The symptoms in tuberculosis of bones and joints depend upon the extent, the duration and location of the process. Symptoms characteristic of the disease in any location are: Impairment of the general health, pain, tenderness, stiffness of the part or muscle spasm, and deformity. In young children the tuberculin test is of value in differentiating other conditions. Early in the disease the Roentgen ray is of little diagnostic value; however, repeated x-rays are of considerable value in studying the progress. With early diagnosis and proper treatment the prognosis in the majority of cases is fairly good. However, a certain amount of deformity usually remains. This is produced by a partial or complete fibrosis or bony ankylosis of the joint.

As has been previously stated the spine is most frequently involved, this condition having been first described in 1779 by Percival Pott; hence the name "Pott's disease." Two-thirds to three-quarters of a vertebra being of spongy material it is fertile soil for the growth of tubercle bacilli. Disease in this location is facilitated by the vertebræ being in constant motion, even a slight movement in them being produced by respiration when a person is in a recumbent position. The lower dorsal region is most commonly affected, although any region of the spine may be the seat of involvement. Undoubtedly the bodies are first attacked; caseation, cavity and abscess formation soon follow. The result is a kyphosis due to a crushing together of the softened vertebræ. Pott's disease of the cervical region has a bad prognosis as this position favors meningitis.

Kyphosis of rickets, syphilis and malignancy must be differentiated.

Among the first symptoms noted in Pott's disease in children are reflex acts of protection. The child, when walking, steadies himself by taking hold of chairs and other objects and does not venture away from them as most children do. When standing alone or in getting up and down he supports himself by placing his hands on his thighs. In cervical disease he holds his head with his hands. There may be a slight lordosis and a contraction of the psoas muscles, causing the thighs to be drawn up. Often the patient walks on his toes with knees bent in order to avoid jarring. On palpation over the affected part an early angulation may be felt. When the patient bends over the affected vertebræ move *en bloc* instead of separately, this being

one of the most significant signs in making an early diagnosis. The vertebral muscles are spastic, acting as a splint. After the child falls asleep these muscles tend to relax. Their relaxation may produce pain, causing the child to awaken suddenly with a scream. "Night-cries," however, are not as frequent in Pott's disease as in tuberculosis of the hip and other joints. Cold abscesses are common complications of this condition and may be found to point almost anywhere. Spastic paralysis, usually bilateral, due to pressure, is not infrequent. Strange as it may seem this paralysis is seldom permanent.

There are no cardinal symptoms in tuberculosis of the hip. The onset is usually insidious. As a rule the first evidence is a limp, intermittent in character. This is the result of an effort to prevent shock. Pain is very variable, although commonly severe. Motion of the hip up to a certain degree is painless, while motion beyond this point produces marked muscle spasm and excruciating pain. Muscle spasm is the first symptom to appear and the last to leave. It is so great at times that an anesthesia may be required to determine whether or not there is actual fixation. Tenderness may be elicited in Scarpa's triangle. Later there is flexion of the hip, tilting of the pelvis and a shortening of the leg, which is invariably flexed and abducted, showing either real or apparent shortening. Atrophy of the hip and thigh region is an early and constant sign.

As tuberculous involvement of the knee joint is very similar to the process when it occurs in other joints, a description of the first condition will serve as typical also for the latter. The joint becomes enlarged, spindle shaped, tender to the touch and painful on motion. Instead of the usual erythema associated with swelling, the skin about the joint remains white— thus the name "tumor albus." The onset is gradual, pain and limping first occurring after exercise, later becoming almost constant. The knee is held in flexion, motion producing muscle spasm and pain. The effusion does not yield to ordinary treatment. A certain amount of atrophy and stiffness remain after the acute process has subsided.

The present trend of treatment of tuberculous bone and joint conditions, particularly in children, is to try conservative medical measures before resorting to radical surgery. Of course, whenever it is possible to operate and remove a focus of infection such procedure is justifiable, but it has been found that children who do not respond to medical treatment also do poorly when treated surgically. The essentials of treatment are: Rest, fresh air, proper food and light. Rest means conservation of strength and energy as well as rest locally through fixation of the diseased part. Fixation is best produced by splints and braces rather than plaster casts which prevent the affected part from being exposed to the sunlight. Albee's operation on the spine is never indicated in children. Bier's hyperemia has been suggested in the treatment of diseased joints but its use is now being discarded. Rid-

lon, speaking of tuberculin, says, "In careful hands it is a harmless method of treatment." Of all recent methods, in addition to building up the child's health, the light treatment suggested by Rollier has proved the most beneficial and has produced gratifying and early results.

LABORATORY METHODS

Tuberculin Tests.—Since 1907, when von Pirquet published his results obtained by cutaneous vaccination with tuberculin, this agent has been used in many different forms, for diagnosis and treatment. Subcutaneous, intra-cutaneous, cutaneous, percutaneous, boring, needle-scratch, sandpaper, inhalation, intratracheal, conjunctival, suppository, vaginal and numerous other methods have been employed. Clinical experience has proven that for diagnostic purposes the intracutaneous test of Mantoux is by far the best of the group, outranking even the cutaneous test of von Pirquet. The skin reactions obtained with both of these methods are relatively specific. Positive reactions indicate infection with the tubercle bacillus and bear no relation to the activity or extent of the process. The injection of tuberculin into the system may be attended by three types of reaction, local, focal and general. The local reaction occurs about the site of injection and is characterized by swelling, redness and tenderness on palpation within twenty-four hours. The acute stage may last for twenty-four to thirty-six hours and then the swelling recedes, pain disappears and the inflammatory redness is gradually replaced by brownish discoloration of the skin over the involved area. Desquamation follows and within a month, as a rule, all traces of the local reaction have disappeared. Occasionally during the acute stage the center may become necrotic but the resulting ulcer readily responds to treatment and heals with very little scarification. Cutaneous tests may be followed by a lymphangitis which is thought by some authorities to indicate an active focus of lymph-node origin.

The focal reaction occurs about the site of infection and is very hard to detect. Experimental study has shown that it is in the nature of an inflammation about the site of the tubercles. Depending upon the activity of the lesion the focal reaction may last for two to four hours and is followed by a period of absorption.

The general reaction coincides with the two preceding reactions. The patient complains of headache, nausea, chills, fever, and muscular pains. Pains in the joints appear within twelve hours or less if the dose has been large enough to cause a general reaction. The duration of this type of reaction averages about eight hours.

Negative tuberculin tests should be repeated, since in the following instances allergy is encountered:

1. During the period of incubation of tuberculosis
2. During the period of extension and cachexia
3. Menstruation
4. During acute illnesses such as pneumonia, grip, pertussis, etc.
5. During intensive tuberculin treatment

The technic of the Mantoux test is as follows: The skin of the inner surface of the forearm is cleaned with alcohol, then with ether, and 0.1 c.c. of a solution containing 0.0001 gram of old tuberculin per c.c. is injected from a tuberculin syringe through a fine needle, preferably a No. 26, which has been inserted *into* but not *under* the skin. When positive the reaction appears in six to eight hours, reaches its maximum in twenty-four hours, and consists of infiltration, hyperemia, and occasionally vesiculation. Readings are made at intervals of one, two and seven days following injection when the area of infiltration and the degree of inflammation are noted. At the time of injection a control of 0.1 c.c. of normal saline is similarly introduced into the skin.

The technic of the cutaneous method of von Pirquet is as follows: The skin on the volar aspect of the forearm is cleansed with alcohol and then with ether. Two small scratches about 3 inches apart are then made through the skin, care being taken to avoid drawing any blood. On one scratch a drop of old tuberculin is placed and allowed to dry. On the other scratch a drop of normal saline is placed and allowed to dry. Both spots are examined at the end of one, two, and seven days and the degree of reaction noted. Considerable experience is needed in interpreting these reactions but those under 5 millimeters in diameter should be regarded as doubtful.

While the Mantoux test is more difficult to perform than the von Pirquet, its use is advised because of its higher grade of sensitivity. A comparison of the two tests by capable observers has time and again shown the greater accuracy of the Mantoux test in tuberculous individuals. The significance of positive tuberculin tests in infants as determined by Bartlett and Wollstein is worthy of note. Their conclusions are as follows:

1. In 75 per cent of infants under six months without evidences of tuberculosis, fatal tuberculosis will develop within the first year of life.

2. In similar cases between six and twelve months, 50 per cent will develop fatal tuberculosis within one year.

3. In similar cases between one and two years, from 25 to 50 per cent will develop the disease but the prognosis is not uniformly fatal.

ROENTGENOLOGY

In the diagnosis of juvenile tuberculosis the x-ray is of great importance as a means of demonstration. It is essential that good technic be observed in order to obtain satisfactory plates which will not only show the extent of the pathology but serve as records for future reference. Another primary requisite is that the plates be read by a person skilled in the interpretation of skiagrams (x-rays). The x-ray may show gland involvement even before they have reached sufficient size to cause cough, dyspnea, or other pressure symptoms and when too small to cause a D'Espine's sign or appreciable dulness. The x-ray, however, is of value only when the clinical findings are used in conjunction with it.

Hilus.—This type is most frequently found in debilitated children with a history of exposure to tuberculosis. Fluoroscopy in many instances brings out the shadows of the enlarged glands but plates bring out the finer details. Not all enlarged glands are shown by x-ray; to be seen they must have density sufficient to obstruct the path of the rays. On the other hand, not all enlarged glands that show on x-ray are tuberculous. Subacute and chronic upper respiratory infections, chronic heart conditions, status lymphaticus, etc., may cause an enlargement of the glands at the hilus.

In hilum tuberculosis the glands at the roots of the lungs and the bifurcation of the trachea are seen to be enlarged and more or less surrounded by an opacity due to vascular engorgement and inflammatory reaction. The tracheobronchial glands show as shadows outside and parallel to the sternum from the clavicle down towards the hilum across the posterior second, third and fourth interspaces and are best seen on the right side. The bifurcation glands are best seen with an oblique position. Because of the pressure incident to the reaction at the root the bronchi are most prominent. Frequently in that portion of the parenchyma of the lung drained by the enlarged glands a faint flufflike area of infiltration can be made out.

The x-ray should be repeated from time to time as a check upon the disease process. Extension is usually indicated by the appearance of other flufflike areas of infiltration near the first, by a bilateral fanwise spread from the affected glands at the hilus, or by a "budding" process along the bronchial tree. Retrogression is shown by the disappearance of the inflammatory reaction about the glands at the hilum and the discrete sharply outlined appearance of the affected glands incident to their calcification. A chronic hilus condition shows up as a clear wedgelike shadow extending out into each lung, giving rise to a butterfly appearance. In the chronic form there may be involvement of the pleura as shown by the appearance of an effusion or adhesions with resulting displacement of the heart, mediastinum and trachea.

Miliary.—This is characterized by a fine mottling of the entire lung field even up to the pleural surface. The picture has been well termed "snow-flaky." As the process advances the lung picture may become opaque.

Bone.—Tuberculosis of the bone is usually found in the epiphyseal portion. It is characterized by a local rarefaction and destruction of tissue giving a blurred, hazy picture with loss of detail. Frequently there is an effusion into the neighboring joint. The rarefaction in the small bones—carpus and tarsus—may be so severe as to leave them with the same density as the surrounding tissue. Localized pockets in the medulla of the long bones are sometimes seen and cannot be distinguished from osteomyelitis or syphilis. Dactylitis of tuberculous origin shows up as an increase in the diameter of the distal phalanx, with areas of destruction in the medulla, and a characteristic thinning of the cortex. Tuberculosis of the spine begins near the intervertebral disks and in the early stages shows only rarefaction and atrophy. Later there is destruction of the body of the vertebra with absorption and resulting kyphos. A fusiform shadow of an abscess is often seen about the affected vertebra.

TREATMENT

Much consideration has been given to treatment of tuberculosis in adults, while until very recently only little attention has been paid to juvenile cases. For example, we have many institutions in this country for adults suffering from this disease but comparatively few where children may obtain the proper care and treatment. But children in no small measure have been greatly benefited by the many campaigns against tuberculosis which have had only the adult in mind. The results of these campaigns have been very gratifying. Fortunately in recent years more emphasis has been placed upon the importance of treating tuberculous children. Among the more intelligent classes we find a fair knowledge regarding the proper hygiene and care of children which is so important in combating the disease. Due to propaganda, many even among the poorer classes recognize early symptoms which are suggestive and take their children to clinics where early diagnosis may be made and proper treatment instituted. Because of this we now seldom see far advanced cases of suppurating cervical adenitis which our older textbooks describe as being so characteristic. This means that the stress which has been placed upon prevention and early diagnosis of tuberculosis has not been without reward. We still see and probably always will, cases showing little or no resistance to the infection which go on rapidly to a generalized tuberculosis. In such cases treatment will prove only palliative.

Almost daily stories of new remedies and cures for tuberculosis appear in our newspapers. Never yet has any drug proved to be curative. Certain

tonics may be greatly beneficial in building up the child's general health or in alleviating symptoms, but they are only augmentary.

There are four essentials in the treatment of tuberculosis; these are rest, fresh air, proper diet, and medical supervision. Rest includes a period of ten to fourteen hours in bed each night, a rest period before dinner at noon, a two-hour nap in the afternoon and another rest period before supper. When children are not resting, recreation should be supervised; competitive sports and strenuous games should not be permitted, for if a child is allowed to play as he wishes he is very apt to go far beyond his endurance and become exhausted. The excitement of many children's games is so great that the child becomes unnerved and cannot settle down to rest when the proper time comes.

The value of fresh air in treating tuberculosis is so generally known that little need be added concerning it. The tuberculous patient should live and sleep practically out of doors. He soon becomes accustomed to the severest winter weather so that when at all confined he feels stuffy. In this connection sunlight is beneficial especially in treating glandular tuberculosis, sinuses, lupus vulgaris and fistula. The direct rays of the sun may be supplemented by the use of an Alpine lamp, particularly in localities where the days are short and in climates lacking in sunshine. More will be said later regarding sunlight treatment and the benefit of the ultraviolet rays. The diet should be of high caloric value, consisting of simple and nourishing food, of which fresh vegetables, eggs, milk and cream, should constitute the major portion. Highly spiced, fried, and greasy foods and condiments should be avoided. As a rule the outdoor life and fresh air are sufficient to create a keen appetite. Milk and cream or cocoa should be taken in the middle of the morning, in the middle of the afternoon and before retiring. A glass of warm milk, taken just before going to bed, often aids the patient in falling asleep readily. The heartiest meal should be at noon. Meat should be included in at least one meal a day.

Considerable tact and diplomacy are required on the part of the physician in order successfully to treat a patient where little or no medicine is used. Upon the physician's personality and the sympathetic manner in which he listens to minor ailments rests the success of such treatment. A tuberculous patient is particularly subject to colds and minor upsets, necessitating close medical supervision and prompt treatment when these conditions arise. The physician must watch closely the patient's weight and temperature, for these are his guides in determining how much and the nature of exercise in which the patient may indulge. Particular care must be taken to avoid constipation, toward which patients have a great tendency due to inactivity. This condition can usually be avoided by regular habits, by sufficient fluids, especially

milk and water, and by diet, supplemented if necessary by the use of bran and mineral oil.

Many cases of juvenile tuberculosis may be prevented by the exercise of proper care. Sufficient rest, proper food, and fresh air are the essentials in the development of a healthy child. During the day the infant may be warmly wrapped and placed out of doors in the sunshine, while at night the windows of the sleeping room should be open so as to give proper ventilation. The play room should be a light sunshiny room with good ventilation and free from stuffed furniture which harbors dust. It is ideal to have one of the new types of glass windows pervious to ultraviolet rays in the play room. By proper diet one avoids debilitating diseases such as rickets. Only certified or pasteurized milk should be used. A child should be taught when young not to put things in its mouth; sucking "pacifiers" should never be permitted. In avoiding colds and exposure during changeable weather it is important that the child be not overdressed. He should be bathed twice daily, and only his own towels used. Fondling and kissing should not be permitted. Open-air schools should be provided for children who are weakly and special schools for tuberculous children.

The idea of "holiday homes" is said to have originated in Switzerland in 1876. Poor children from the cities were given four to six weeks' vacation on suitable farms during the summer. Later colonies were organized where a large number of children could be cared for in the country. This idea is now universal. In the United States this requirement is met by various fresh air funds and such organizations as the Boy Scouts, Girl Scouts, Y. M. C. A. camps, etc.

Preventoria, where children may be cared for who are under par, yet not definitely tuberculous, are increasing in numbers. European countries have shown much foresight in establishing many such institutions. In 1903 Grancher founded "The League of Prevention of Children from Tuberculosis." This organization aims to relieve tuberculous parents of the burden and care of their children, when it finds them doomed to be much neglected because of the sickness of father or mother. Its main object is to remove the children from the danger of daily infection. The idea of taking children of consumptive parents to other surroundings has largely been promoted by the Swedish Anti-Tuberculosis Association, which has gone to the extent of making it obligatory that children under three years of age be removed from homes where one or the other parent is suffering from tuberculosis. Such children are either placed in institutions or foster parents are found for them. Such a procedure is a most important measure in controlling the spread of the disease. Rigid supervision of all cases is necessary. In 1903 Germany enacted a law requiring examination of all members of a family in which a case of tuberculosis is found.

The treatment of glandular tuberculosis has become largely a medical problem. For many years radical surgery has been advocated in cervical adenitis, but at present it is growing in disrepute, for cases treated surgically progress no more favorably than those treated medically. The same may be said also of cases treated with radium or by x-ray. Glands which have broken down and become fluctuant should never be opened to give drainage; they may be aspirated, a needle being inserted through healthy tissue.

The most important feature in treating glandular tuberculosis is the building up of the child's general health. This is done by removing foci of infection, such as tonsils and adenoids, which tend toward further impairment of the child's health. Most children may be best cared for in a sanatorium where they may live out of doors and be under ideal hygienic surroundings. Cases of early tuberculous adenitis when thus treated rarely go on to advanced stages. Those which do have low resistance to the infection. In fact it is persons in this class who make up the mortality lists under any form of treatment. In addition to building up the general health of these children the local condition is benefited by exposure to sunlight or the Alpine lamp; by iodin, most suitably given in the form of syrup of hydriodic acid, and by cod-liver oil which aids in the calcium metabolism.

Heliotherapy.—Heliotherapy now plays a very important rôle in the treatment of selected cases of extrapulmonary tuberculosis. Since juvenile tuberculosis is usually of the extrapulmonary form this method is particularly applicable to cases occurring during childhood. The first systematic study of this method was made by Finsen who in 1895 founded the Light Institute in Copenhagen for the treatment of lupus vulgaris and other diseases. In 1903 Rollier founded his famous clinic at Leysin for surgical tuberculosis. The development of heliotherapy as a clinical aid is due more to him than to any one else. It is believed that best results are obtained when the treatment is carried on at high altitudes, because at low levels many of the sun's rays are absorbed by moisture and dust particles in the air surrounding our cities. Where there is not sufficient sunlight or satisfactory facilities for exposing patients to the direct rays of the sun the ultraviolet rays derived from the Alpine lamp may be utilized. The beneficial results obtained from this form of therapy are well expressed in the old Italian proverb, "Where the sun does not enter, the doctor goes."

Heliotherapy produces an increased metabolic rate, affecting particularly the calcium metabolism. Experimentally in animals a pulmonary congestion has been found following exposure to ultraviolet rays. Such a condition would predispose to pulmonary hemorrhage; therefore this method is contraindicated in active pulmonary conditions. A permanent pulse rate of over 130 or a persistent temperature of 101.5° F., non-compensated valvular heart lesions, anemia, emphysema, diabetes and psychoneurosis are also contra-
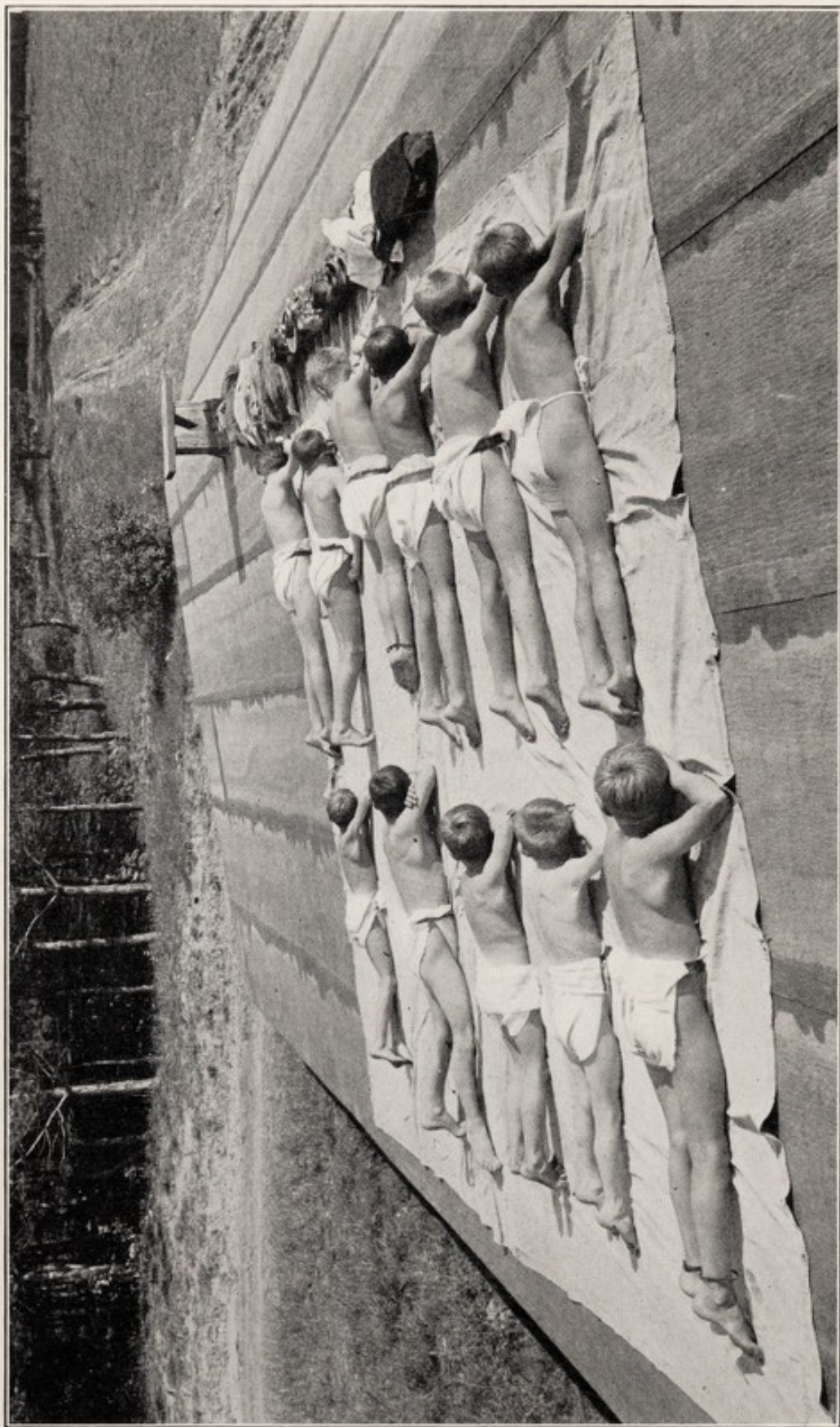
FIG. 23.—TUBERCULOSIS.
Sunlight treatment, Albany Hospital Tuberculosis Sanatorium.

indications. The most striking results from this treatment are found in cases of lupus vulgaris, all forms of glandular, intestinal and peritoneal tuberculous involvements and in tuberculous conditions of bones and joints. In bone and joint conditions surgical intervention is indicated chiefly in dealing with deformities. The light treatment produces a rapid expulsion of sequestra. Tuberculin treatment has never proved sufficiently efficacious to

FIG. 24.—TUBERCULOSIS.
Quartz light treatment.

warrant its use. Cases of tuberculous peritonitis are particularly amenable to heliotherapy. When there is an ascites present paracentesis in addition to light treatment produces the best results.

Rollier has developed a definite technic for the use of heliotherapy. The individual differences in the adaptability of patients should be carefully considered. Care should be taken to avoid chilling and unnecessary exposure to winds. Exposure always begins with the feet, legs, thighs, abdomen and chest in the order named. The head is covered in order to protect it from the direct rays. The length of exposure is gradually increased until the patient finally lies with the entire body exposed from a few hours to almost all day

in either summer or winter. Essentially the same technic is employed by all workers.

For some years Calmette has been working on a vaccine which may prove to be a great factor in reducing the incidence of juvenile tuberculosis, but as yet his work is still in the experimental stage. He made 230 successive cul-
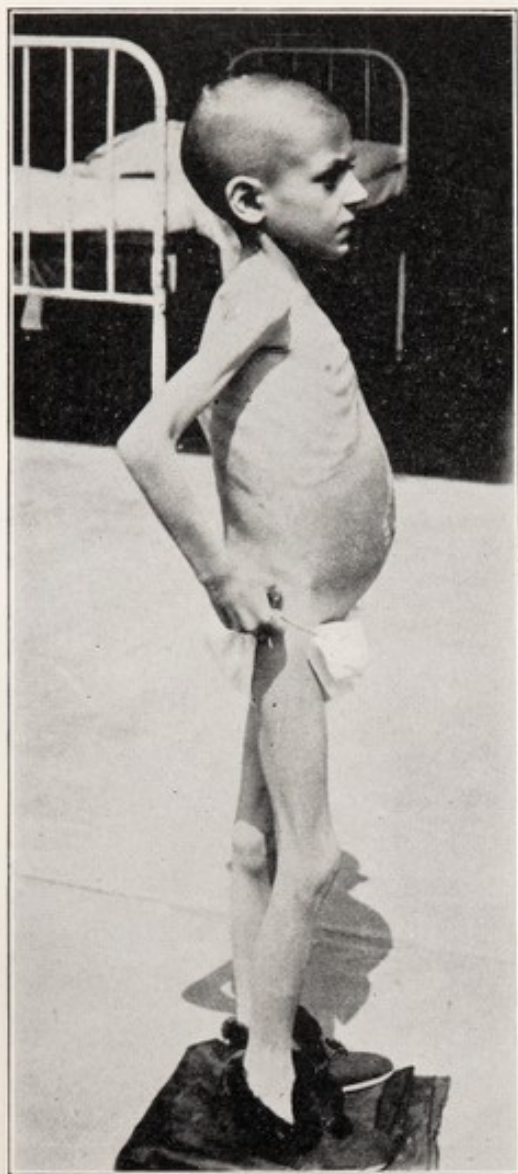
FIG. 25.—TUBERCULOUS PERITONITIS, BEFORE HELIOTHERAPY.

FIG. 26.—TUBERCULOUS PERITONITIS, AFTER HELIOTHERAPY.

tures of tubercle bacilli of bovine type which became thoroughly non-pathogenic, yet still capable of producing "immune-bodies." A positive complement test is obtained in animals inoculated with this material fixation. He designated this modified strain of bacillus as "B.C.G." and found that inoculations of 50 to 100 milligrams of "B.C.G." into the areolar tissue of young calves creates an immunity which will resist perfectly intravenous inoculations of 5 milligrams of virulent bovine bacilli for as long as eighteen

months. Similar doses of virulent bacilli proved fatal to controls in six to eight weeks. The "B.C.G." does not in any way disturb the health of vaccinated calves nor give rise to any single focus of infection. Similar results have been obtained in rabbits and guinea-pigs given "B.C.G." either subcutaneously, intravenously or orally. The vaccine is efficacious only in animals free from tuberculosis. Overdoses produce an adenitis appearing about the eighth day, which disappears completely after one month. If by this method tuberculosis in cattle can be prevented a great source of infection will be eliminated. The British Government has endorsed this method and recommends its use.

Calmette, however, has gone still further in his experiments. He has given his "B.C.G." vaccine to several thousand infants, each of whom was fed from a spoon three doses of 2 milligrams each one-half hour before nursing during the first nine days of life. These children have been followed closely and have developed normally without derangement of health. Insufficient time has as yet elapsed to determine final results of these experiments, but the outlook is very promising. The French Government after a thorough investigation has become convinced of its value and urges its general adoption.

THE SEROLOGY OF TUBERCULOSIS

The reports written on the serology of tuberculosis are legion. For years workers in this field have tried to produce a laboratory test of clinical import in the diagnosis, prognosis and treatment of the disease, but to date none has proved satisfactory. Test after test has been advanced and has been followed by numerous modifications which have failed to produce the desired result. The agglutination, precipitin, and opsonic index reactions have never gained much favor as aids in the diagnosis of tuberculosis, but the complement fixation test is still the subject of a great deal of research. In general the technic of the test follows that of the Wassermann reaction but so many "refinements" have been introduced by various workers that it is difficult to confirm results from different laboratories. Another great difficulty which detracts from the usefulness of this reaction is the lack of a standardized antigen, practically every complement fixation worker modifying the antigen used. In this country those advocated by Besredka and by Petroff are the most commonly accepted. Park and Williams report that with a suitable antigen they have obtained positive complement fixation reaction in from 75 to 90 per cent of clinically active pulmonary cases. Cooke, working with children, reports that in manifest cases of tuberculosis he obtained no reaction with the complement fixation test in children less than one year old, but in the second to the fourth year he obtained 40 per cent positive reactions, in the fourth to the sixth year he obtained 56 per cent,

while in children over six years he obtained 80 per cent positive reactions. The same percentages were obtained in children with marked tuberculosis, while in suspects he obtained positive reactions in 50 per cent of the cases. From these figures Cooke concludes that in children a positive complement
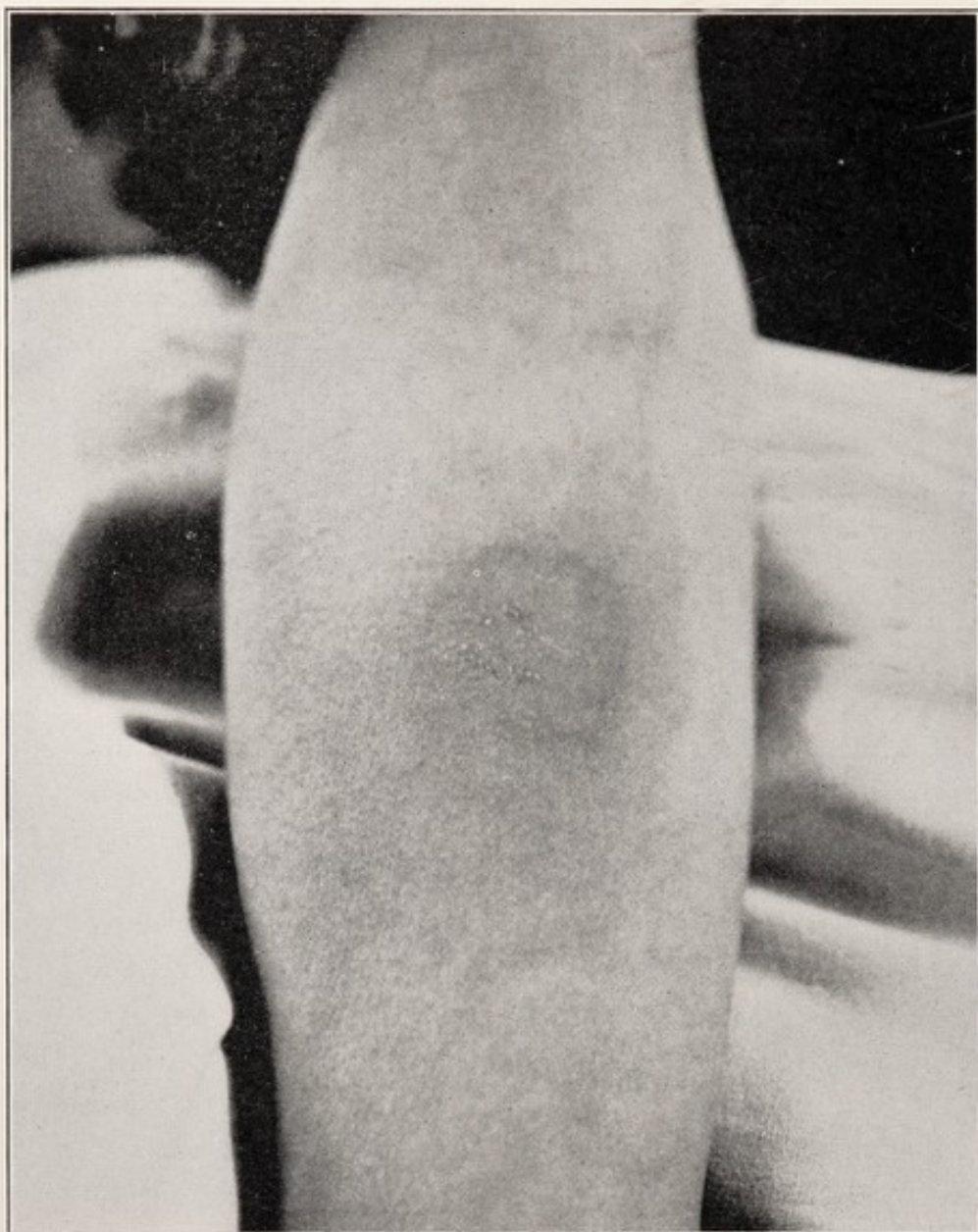
FIG. 27.—STANDARD TUBERCULIN FRANKFURT 1 : 1,000 INTRACUTANEOUS INJECTION. Twenty-four-hour reaction.

fixation reaction indicates pathologic if not clinical activity. Josewich and Grave, after a practical study of the reaction, conclude that it indicates tuberculosis either manifest or concealed; that it is superior in accuracy and practical application to the ring or flocculation tests; that the reaction is specific but of no value in prognosis.

Various other tests have from time to time been brought forth in the

hope of diagnosing active tuberculosis. The serum precipitin test, the tuber-cumet and ring tests, serum agglutination tests, the opsonic index test, serum flocculation test, Matefy's globulin test, erythrocyte suspension stability test and others have been advanced as aids in the diagnosis of active tuberculosis. The following extract from Volume II of the Trudeau Foundation Studies

FIG. 28.—STANDARD TUBERCULIN FRANKFURT 1 : 1,000 INTRACUTANEOUS INJECTION.
Forty-eight-hour reaction.

summarizes the present status of serum diagnosis of tuberculosis: "In the enumeration of serum reactions that have diagnostic value it is evident that the Bordet-Wassermann tuberculosis test has thus far proven the best in confirming clinical disease. The delicacy of the test for precipitin has been nearly as great, but none of the reactions has paralleled either the symptoms of the disease or the tuberculin reaction in the skin. The serum reactions, however, when positive, more often indicate clinical tuberculosis and do not persist long after symptoms cease."

PUBLIC HEALTH REGULATIONS

Every practicing physician should be familiar with the public health law as it affects tuberculosis patients. The New York State Department of Health requirements are typical of what is required by many states in this country. The Sanitary Code states "tuberculosis is hereby declared to be an

Fig. 29.—Standard Tuberculin Frankfurt 1 : 1,000 Intracutaneous Injection. Same patient four days after injection.

infectious and communicable disease, dangerous to public health. It shall be the duty of every physician in the State to report by telephone or in person or in writing on the tuberculosis report card the name and address of every person suffering from tuberculosis *of any type*, within twenty-four hours after such fact comes to the knowledge of the physician." This report is to be made to the local health officer. In addition to this provision for the reporting of cases any physician may report to the health officer any person coming under his casual observation who appears to be suffering from tuberculosis. The health officer will provide containers to physicians for the laboratory examination of sputum. The health officer is required to

promptly make a report of the results of such examination free of charge to the physician who made the application.

Tuberculosis records are confidential and no one is permitted to inspect them other than the health authorities or such persons as may be authorized to do so by the State Commissioner of Health.

Fig. 30.—Standard Tuberculin Frankfurt 1 : 1,000 Intracutaneous Test.
Same patient, forty-eight-hour reaction, showing excessive reaction, marked redness and swelling. Blisters in center later followed by necrosis.

Following the vacation of any apartment or premises by a person having tuberculosis through death or otherwise, it is the duty of the attending physician to notify the health officer in order that provision for cleansing, disinfecting or renovating may be carried out.

Provision is made in the law for the control of patients having tuberculosis who are careless in the disposal of their sputum, saliva or other bodily secretions or excretions. When a patient becomes careless and dangerous so as to be a public menace, the physician should notify the health officer of such fact so that proper legal action may be taken. The magistrate is

empowered to commit such patients to county tuberculosis hospitals. New York State maintains a State Hospital in the Adirondacks for the treatment of incipient pulmonary tuberculosis. Physicians desiring hospitalization of appropriate cases in this institution make application to the health officer of the locality in which the patient resides who arranges for the admittance.
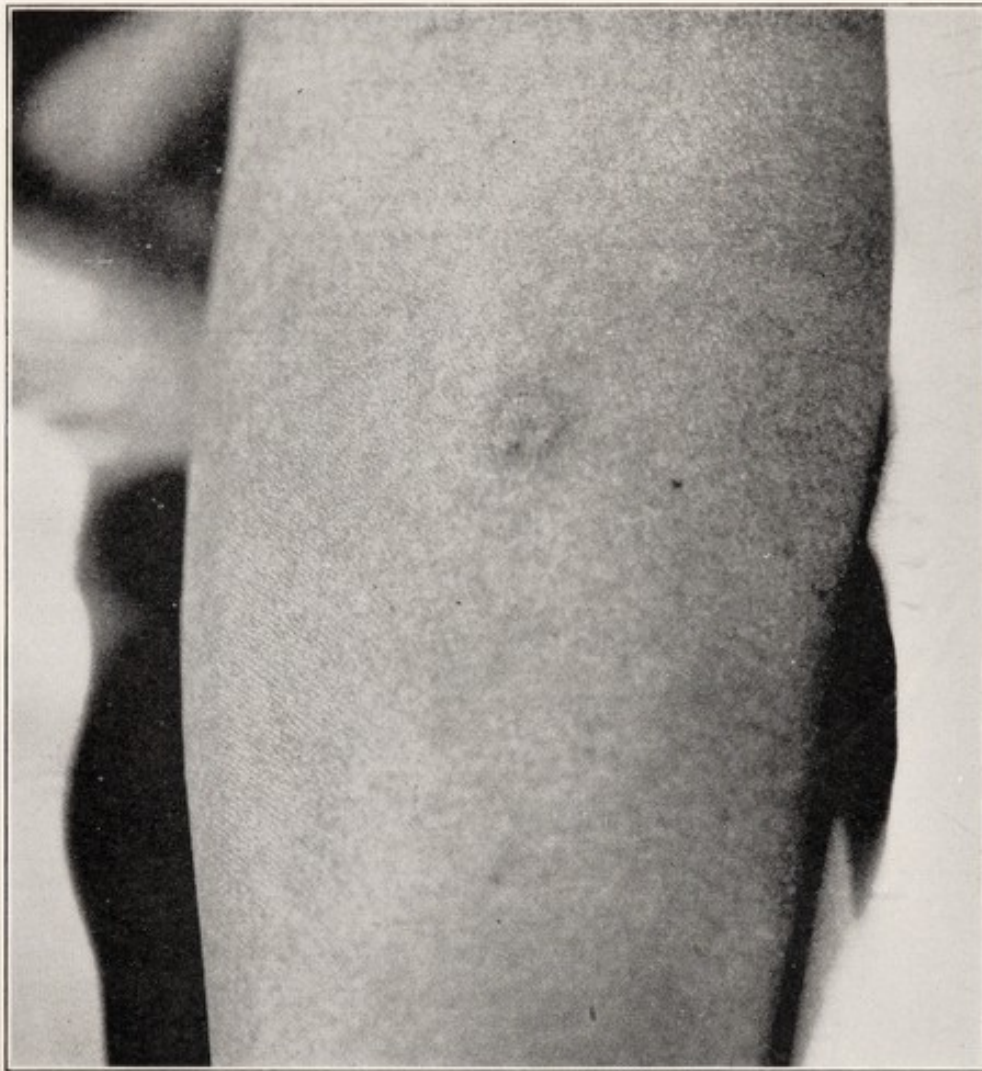
FIG. 31.—NEW YORK STATE LABORATORY TUBERCULIN 1 : 1,000 INTRACUTANEOUS INJECTION. Forty-eight-hour reaction.

The attending physician is expected to report the recovery of any of his patients having tuberculosis to the local health officer and such person is relieved from any of the requirements of the law.

Physicians who fail to report cases, or make false reports, or neglect to carry out any of the precautions necessary to prevent the spread of infection, shall be deemed guilty of a misdemeanor and on conviction thereof shall be subject to a fine of not more than one hundred dollars.

The New York State Department of Health conducts diagnostic chest clinics in communities which have no special facilities for establishing the

early diagnosis of tuberculosis. These clinics are conducted on a strictly consultation basis. Only persons presenting an admission card signed by their family physician or the health officer may be examined at these clinics. The evidence elicited by the history, physical examination and x-ray is compiled by the examining physician and a detailed report is sent at the earliest opportunity to the family physician. These clinics have the support of the

FIG. 32.—TYPICAL REACTION OF INTRACUTANEOUS TEST, OLD TUBERCULIN I : 1,000.

local physicians and are a great aid in establishing an early diagnosis of tuberculosis.

The Committee on Standard Regulations for the Control of Communicable Diseases outlines the following concerning the present status of tuberculosis:

Tuberculosis (Pulmonary)

1. INFECTIOUS AGENT.—Tubercle bacillus (human), *Mycobacterium tuberculosis (hominis)*.

2. SOURCE OF INFECTION.—The specific organism present in the discharges, or articles freshly soiled with the discharges from any open tuberculous lesions, the most important discharge being sputum. Of less importance are discharges from the intestinal and genito-urinary tracts, or from lesions of the lymphatic glands, bone, and skin.

3. MODE OF TRANSMISSION.—Direct or indirect contact with an infected person by coughing, sneezing, or other droplet infection, kissing, common use of unsterilized food utensils, pipes, toys, drinking cups, etc., and possibly by contaminated flies and dust.
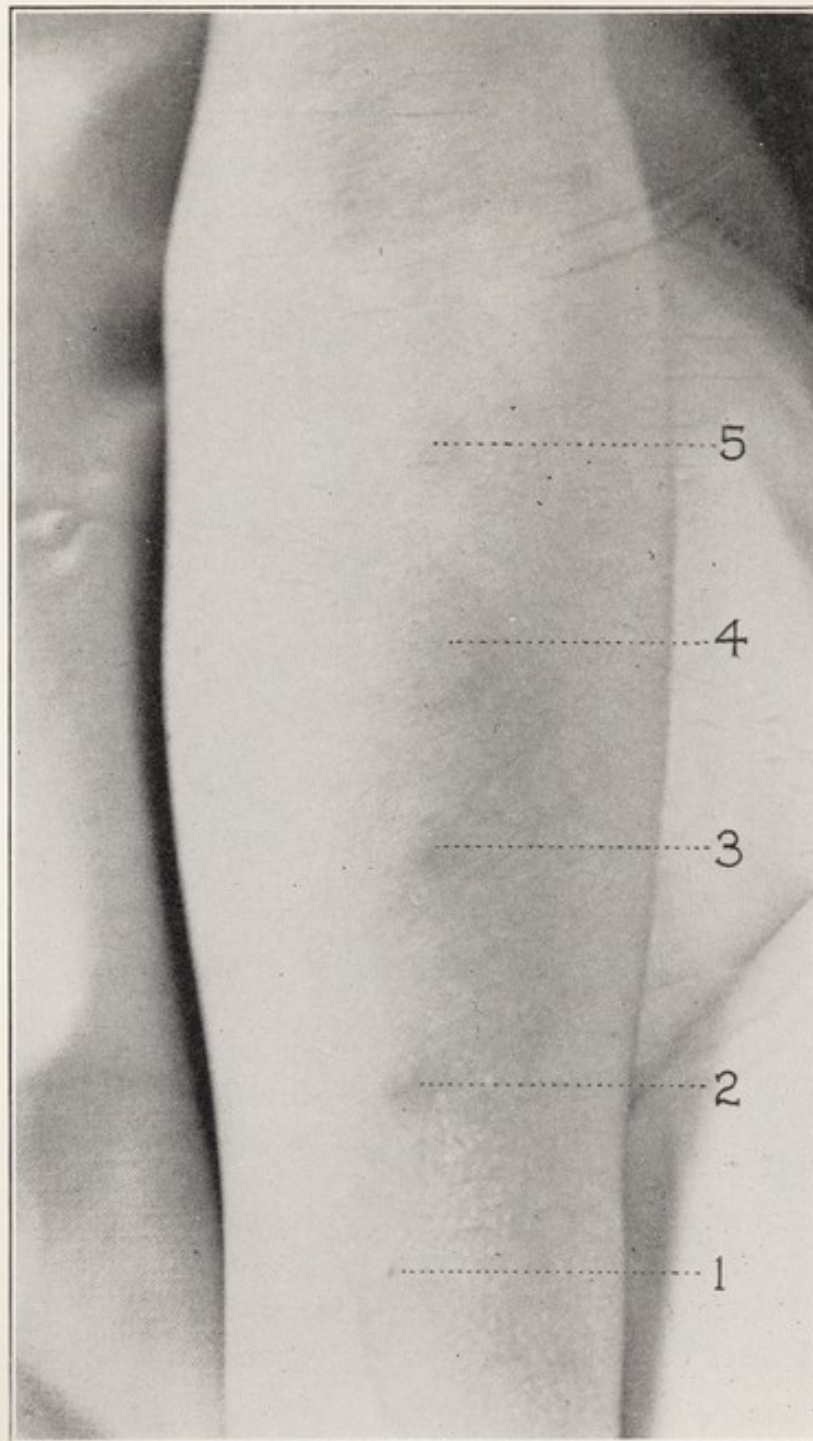
FIG. 33.—INTRADERMAL TUBERCULIN TESTS WITH OLD TUBERCULIN AT DIFFERENT
DILUTIONS.

1. Normal salt control.
2. 1 : 10,000 dilution.
3. 1 : 5,000 dilution.
4. 1 : 2,000 dilution.
5. 1 : 1,000 dilution.

4. INCUBATION PERIOD.—Variable and dependent upon the type of the
disease.

5. PERIOD OF COMMUNICABILITY.—Exists as long as the specific organism
is eliminated by the host. Commences when a lesion becomes an open one—
i.e., discharging tubercle bacilli, and continues until it heals or death occurs.

6. METHODS OF CONTROL

    (*a*) The infected individual and his environment

        1. *Recognition of the Disease.*—By thorough physical examination supplemented by use of the x-ray and specific skin reactions when necessary and confirmed by bacteriological examinations of sputum or other materials.

        2. *Isolation* of such "open" cases as do not observe the precautions necessary to prevent the spread of the disease.

        3. *Immunization.*—None.

        4. *Quarantine.*—None.

        5. *Concurrent disinfection* of sputum and articles soiled with it. Particular attention should be paid to prompt disposal or disinfection of sputum itself, of handkerchiefs, cloths, or paper soiled therewith, and of eating utensils used by the patient.

        6. *Terminal Disinfection.*—Cleaning and renovation.

    (*b*) General measures

        1. Education of the public in regard to the dangers of tuberculosis and the methods of control, with especial stress upon the danger of exposure and infection in early childhood.

        2. Provision of dispensaries and visiting nurse service for discovery of early cases and supervision of home cases.

        3. Provision of hospitals for isolation of advanced cases, and sanatoria for the treatment of early cases.

        4. Provision of open-air schools and preventoria for pretuberculous children.

        5. Improvement of housing conditions and the nutrition of the poor.

        6. Ventilation and elimination of dust in industrial establishments and places of public assembly.

        7. Improvement of habits of personal hygiene and betterment of general living conditions.

        8. Separation of babies from tuberculous mothers at birth.

Tuberculosis (other than Pulmonary)

    1. INFECTIOUS AGENT.—Tubercle bacillus (human and bovine), *Mycobacterium tuberculosis (hominis et bovis).*

    2. SOURCE OF INFECTION.—Discharges from mouth, nose, bowels, and genito-urinary tract of infected humans; articles freshly soiled with such discharges; milk from tuberculous cattle; rarely the discharging lesion of bones, joints, and lymph nodes.

    3. MODE OF TRANSMISSION.—By direct contact with infected persons, by contaminated food, and possibly by contact with articles freshly soiled with the discharges of infected persons.

    4. INCUBATION PERIOD.—Unknown.

    5. PERIOD OF COMMUNICABILITY.—Until lesions are healed.

    6. METHODS OF CONTROL

        (*a*) The infected individual and his environment

1. *Recognition of the Disease.*—Clinical symptoms confirmed by bacteriological and serological examinations.

2. *Isolation.*—None.

3. *Immunization.*—None.

4. *Quarantine.*—None.

5. *Concurrent Disinfection.*—Discharges and articles freshly soiled with them.

6. *Terminal Disinfection.*—Cleaning.

(*b*) General measures

1. Pasteurization of milk and inspection of meats.

2. Eradication of tuberculous cows from milch herds used in supplying raw milk.

3. Patients with open lesions should be prohibited from handling foods which are consumed raw.

CHAPTER XXII

INFLUENZA

Definition.—Influenza is a communicable disease which appears both sporadically and in widespread epidemics. This disease, which affects persons of all ages, is caused by a specific organism and is characterized by fever and prostration, with inflammation of the respiratory and gastro-intestinal tract. One attack of influenza does not afford immunity to subsequent attacks. It has a high morbidity, low mortality, and spreads rapidly.

Synonyms.—Grip, infectious cold, epidemic grip, epidemic influenza; la grippe.

History.—This is a disease known to antiquity. Medical literature between the years A.D. 877 and 1481 refers to epidemics of what was probably influenza. A pandemic occurred in Europe in 1510, of which authentic and detailed accounts have been preserved. Heberden wrote on influenza in 1775. The first recorded epidemic in America occurred in 1627. Since then there have been a number of widespread outbreaks, the most extensive and important of which appeared in the years 1918 and 1919.

Epidemiology.—Great pandemics of this disease have swept the world at irregular intervals. Each epidemic seems to have three distinct waves. The first is generally mild and lasts from three to six weeks. The second is more severe and lasts longer, while the third affects fewer persons, lasts longer than either the first or the second wave, is more severe, and is more apt to be associated with complications. The intervals between these waves in any particular epidemic are irregular and depend probably on the available susceptible material and the routes and methods of transportation and communication.

This disease seems to be endemic in certain portions of the world. No age is immune to influenza, though cases are comparatively rare in early infancy. In the 1918 epidemic in London it was found that among forty-nine infants breast-fed by mothers suffering from the disease, 15 to 30 per cent contracted the disease, while among bottle babies exposed to their mother's illness 54 per cent were affected. Infant asylums and children's hospitals are particularly liable to be hard hit by the disease. The highest incidence is between the ages of five and forty.

Hirsch studied 175 epidemics and found that over half occurred in the

spring months, with the winter months second in frequency, but the disease is more severe and the mortality is greater in the colder weather.

All races are affected, but negroes and Italians seem to be more susceptible and their mortality rate is higher. One attack does not give protection against another. Cases have been reported which have been affected on two or more occasions in the same epidemic. Macewen observed that boys in four schools in England who were attacked in the first wave were less susceptible to the third wave. A number of authorities believe that there is an immunity or lessened susceptibility for three to five months. Some persons appear to enjoy a natural immunity to the disease.

It is now generally conceded that influenza is spread by human intercourse. The infecting agent appears to be transmitted largely by coughing, sneezing, or what is now termed "spray" infection.

Etiology.—Pfeiffer, in 1889, isolated a bacillus which bears his name and is now quite generally accepted as the specific organism of this disease. Some authorities, while not denying its usual presence in typical cases, believe it to be a secondary invader and that the disease is actually caused by a filtrable virus. Pfeiffer found the bacillus in pure culture in from 90 to 100 per cent of cases in the early stages of the disease. It has been isolated from the blood stream, and monkeys inoculated with it have developed the disease. This bacillus is a very short and small rod-shaped organism, non-motile and non-spore-bearing. It does not stain well with the ordinary aniline dyes but does stain readily with a weak carbol-fuchsin solution. Pfeiffer used blood agar as a medium and colonies in the form of very small circular dots appear in twenty-four hours at incubator temperature. Smear diagnosis is not reliable.

This bacillus is found not infrequently in the nose and throat of healthy persons—"influenza carriers." Park claims that 50 per cent of the population harbor the influenza bacillus in winter.

Other bacteria which are often found in conjunction with the Pfeiffer bacillus and may act as secondary invaders are, pneumococcus, type IV, *Streptococcus hemolyticus* and *viridans* and the *Micrococcus catarrhalis*.

Any condition in the surroundings and personal hygiene which tends to lower the body resistance is a factor in the spread of the disease. For example, overheated houses, insufficient ventilation, carelessness in dressing, improper diet, especially in regard to sweets, exposure to drafts, wet feet, etc., tend to make a person more susceptible.

Pathology.—There are no definite lesions characteristic of influenza and patients do not die of the simple forms, but from complications which show nothing distinctive from lesions caused by other organisms. Holt stated that the influenza bacillus was more frequently associated with inflammation of the lower respiratory tract. It is found in comparatively

few cases of inflammation of the nose, throat, and accessory sinuses. In young children bronchopneumonia is the most frequent type of inflammation of the lungs and the influenza bacillus is invariably associated with other organisms.

Symptoms.—The period of incubation is short, rarely over two days. The onset is abrupt and acute as a general rule. The first symptoms are not unlike those accompanying any of the other acute febrile infections. A great variety of symptoms may be present and any organ or tissue of the body may be involved. The disease is liable to be more severe in its onset and course in young children. It may be ushered in with convulsions in association with the fever. The upper respiratory passages and the conjunctivæ are affected first and the early symptoms are accompanied by extreme prostration. The fever is a constant symptom, is usually high with slight morning remissions, and may reach 105° or 106° F. Children also complain of pain in the back and in the muscles of the arms and legs. The leukocyte count is not increased unless complications are present and in the simple forms of the disease there may be a leukopenia. Skin rashes in the form of erythema or urticaria are not uncommon and may resemble scarlet fever or measles. The disease when uncomplicated runs its course in from three days to a week.

Four fairly distinct types of the disease have been described, based on the most prominent symptoms found in an individual case, but cases may show symptoms embracing two or more of these four types.

The *respiratory* type is the most common. The mucous membrane of the upper and lower respiratory tracts may be affected. Conjunctivitis and swelling of the eyelids are usual, and otitis media is relatively frequent, especially in young children. A hacking, continuous, and distressing cough is always present and may occur in paroxysms, closely resembling whooping-cough. A severe form of laryngitis, difficult to differentiate from diphtheria, is not infrequent and may threaten life. Epistaxis is common and the cervical lymph-nodes are often enlarged. The lower air passages are involved in the most serious cases. There may be simply a bronchitis, but this may extend into the smaller tubes. This capillary bronchitis or bronchopneumonia is a very serious complication in young infants and children. Large areas of consolidation are infrequent and the course of the disease is irregular, lasting in some cases only a few days, while in others it may be prolonged for weeks.

The lesions vary according to the organisms that are present as secondary invaders. Empyema and pleurisy are not more commonly found as complications than in bronchopneumonia due to other causes.

The *gastro-intestinal* type is more frequent in young children, the most prominent symptoms being vomiting, diarrhea, fever and prostration with

usually no involvement of the respiratory tract. Muscular pains and abdominal tenderness are generally present. The diarrhea may be severe. The stools are watery, contain mucus, and are tinged with blood. In some cases the infection extends into the common duct, and jaundice results. The tongue is coated and there is a loss of appetite.

The *nervous* type is common in young children. Headache is a distressing symptom and convulsions are not infrequent. There may be delirium or coma, restlessness, irritability, and insomnia. The extreme prostration is characteristic and the temperature usually very high. Meningeal symptoms, such as stiff neck, Kernig and Babinski signs, tache cérébrale, etc., may be present and the lumbar puncture show a clear fluid under pressure but with no globulin or increase in cellular elements. This is called meningism. There are cases of *true* meningitis in which the spinal fluid is cloudy and contains a large number of cells and the influenza bacilli in pure culture. These cases are almost invariably fatal.

The *febrile* type includes those in which there is no localization of the inflammatory processes. The chief symptoms are fever, accompanied with great prostration, loss of appetite and tenderness of the muscles of the back and extremities. Several authors describe a chronic form of influenza. This must not be confused with relapses which are not uncommon. A patient may feel much better and be up and about, only to be suddenly stricken after a few days with another attack of the disease which may be more severe than the first. The temperature in the chronic cases may be elevated for months, the condition resembling tuberculosis.

Psychoses may develop. These are shown by hallucinations, stupor, amnesia, etc. The mind generally returns to its normal condition when the patient recovers strength. Ewald reported a case of a seven-year-old boy suffering from influenza who went to a railroad station and boarded a train instead of going to school and afterwards had no recollection of these acts.

Influenza in *young infants* runs a more severe course than in older children. It is not uncommonly ushered in with a convulsion and high fever. Catarrhal symptoms affecting the eyes, nose, and throat are present and the middle ear is almost invariably involved. Gastro-intestinal symptoms, such as vomiting, diarrhea, and loss of appetite, are common. There may be a very troublesome distention of the bowels. Restlessness, irritability, and great prostration are frequent. The cough is distressing and in severe cases complications of bronchitis and bronchopneumonia occur which are liable to prove fatal.

Complications.—Any tissue or organ may be affected by the organism causing influenza or by the secondary invaders. The most serious complication is pneumonia, but empyema is a dangerous complication in infants.

Tuberculosis may follow influenza or a persistent cough may last for months after a comparatively mild attack.

The heart may show the effect of the toxins, with a resulting myocarditis and endocarditis. Bradycardia is not infrequently present.

There may be a transitory albuminuria, but real nephritis is uncommon. The skin may show various types of eruption and a general furunculosis may develop in young infants.

Diagnosis.—There is no difficulty in making a diagnosis in the presence of an epidemic. The sudden onset, great prostration and weakness, muscular and back pains with or without catarrhal symptoms, point to influenza. But the term influenza is often much abused, being used to cover many inaccuracies in diagnosis. The bacteriological test is of decided value. The smears must be made on blood agar similar to that used in the diagnosis of diphtheria, for a smear on a cover glass direct from the swab is not accurate. The diagnosis in some cases is so difficult it can only be made by exclusion. It seems to be the fashion to call all head colds "influenza" although they may be due to a number of other organisms. Only when the influenza bacillus is the predominating organism is the diagnosis of influenza justified.

Differential Diagnosis.—Influenza with a sore-throat and erythematous rash may simulate scarlet fever. The rash in influenza is of short duration and the skin blanching test is negative. There is no strawberry tongue, the cervical lymph-nodes are not so apt to be enlarged and the rash is not followed with a profuse desquamation.

Measles shows catarrhal symptoms with fever in the stage of invasion and the rash lasts three to four days. Koplik spots are never seen in influenza.

Typhoid fever develops slowly and the typical rose spots, enlarged spleen and positive Widal should distinguish it from influenza. Typhoid in infants often presents many differences from the typical course seen in adults, and without the blood tests it is sometimes difficult to make a positive diagnosis.

The possibility of a tuberculosis must be considered in some cases, but a negative tuberculin test and a negative x-ray of the chest will be of assistance in reaching a diagnosis.

The presence of a true meningitis or of a meningism can only be determined by lumbar puncture and a cellular and bacteriological examination of the fluid. The type of meningitis will also be determined by the examination of the spinal fluid.

Prognosis.—This is good in simple cases of influenza without complication. Even in these cases in young infants a mastoiditis may follow otitis media and result fatally. The prognosis should be guarded if pul-

monary complications arise. Death results from the complications, not from influenza itself. In young infants who are undernourished the prognosis is not as favorable as in strong, well-nourished babies. The mortality in older children is less than 2 per cent.

The mortality rate of influenza during the ten-year period 1915 to 1925 in the United States shows a tremendous increase in 1918, the year of the widespread epidemic, which did not return to normal until three years later. The rate by ages shows that about the greatest percentage of cases were in infants under one year (Table XXXVIII).

TABLE XXXVII.—INFLUENZA DEATH RATE PER 100,000 POPULATION IN THE UNITED STATES DEATH REGISTRATION AREA AND NEW YORK STATE, 1915-1925

Year	United States Registration Area	New York State	New York City	New York State Exclusive of New York City
1915	16.0	14.3	10.1	18.9
1916	26.5	22.6	16.1	30.0
1917	17.3	16.7	12.2	22.0
1918	300.8	259.1	28.9	294.2
1919	98.8	77.9	86.7	67.6
1920	71.0	56.3	61.9	49.8
1921	11.5	7.3	6.7	8.0
1922	31.4	17.1	15.1	19.4
1923	44.7	23.8	20.0	28.1
1924		10.2	9.4	11.0
1925		12.5	11.3	13.9

TABLE XXXVIII.—INFLUENZA DEATH RATE PER 100,000 POPULATION IN NEW YORK STATE, 1915 TO 1924, ACCORDING TO AGE

Age, Years	Number		Rate		Per Cent of All Cases	
	1915	1924	1915	1924	1915	1924
Under 1	120	121	49.4	51.7	.5	.7
1	34	66	18.3	30.9	.6	2.1
2	16	23	8.1	10.5	.8	1.5
3	10	11	5.1	5.0	.8	1.2
4	6	13	3.2	6.1	.7	1.6
5-9	10	37	1.1	3.5	.4	1.4
10-14	14	16	1.7	1.7	.8	.9
15 and over	1204	834	17.0	10.5	1.1	.7
TOTAL ALL AGES	1414	1121	14.3	10.2	1.0	.8

TREATMENT

Prophylaxis.—The source of infection appears to come from the secretions of the upper respiratory tract and its spread seems to follow lines of

communication and contact with persons infected with the disease. It does not appear to be carried by insects or in food or water. The bacilli can be carried by healthy persons who harbor the germs.

The use of a normal salt solution to cleanse the nose and throat two or three times a day when the disease is prevalent is of decided value and should be strongly urged. The use of a gauze mask is not advisable. Personal hygiene affords protection by increasing resistance, as do good nourishing food, regular bowel movements, plenty of air and sunshine and good ventilation. Children should have sufficient rest and mental and physical fatigue should be avoided. During epidemics children should not be allowed to go to the theater and should be kept away from crowded gatherings. In very severe epidemics it may be advisable to close the day and Sunday schools. As the incubation period is very short and the disease not always recognized in its early and most infectious stages, a single patient might convey the disease to a large number of persons. There are no drugs that have proved to be of special value in preventing influenza. Hexamethylenamin, 3 to 5 grains, well diluted in water, three or four times a day may have some prophylactic value. Quinin and oil of eucalyptol have been recommended.

The use of vaccines prepared from the influenza bacillus, pneumococcus, and streptococcus was resorted to extensively during the great epidemic of 1918-1919, but benefit therefrom was not proved. Prophylactic vaccination against influenza is still in an experimental stage and while it well deserves a trial, other protective methods mentioned above must not be neglected.

General.—Every child suffering from even a mild form of influenza must be put to bed and kept there until several days after the temperature and acute symptoms have subsided. He should be isolated and all discharges from his nose and throat collected on gauze and burned. The room should be well aired. Water should be given freely to dilute and to aid in the excretion of the toxins. Food should not be forced or urged upon the child. When his appetite returns he should have food suitable to his digestive capabilities. The bowels should be kept open.

The fever is usually of short duration and simple sponging or an ice-cap may be sufficient to reduce it. Small doses of antipyrin or phenacetin, 1 to 3 grains, every four hours, are of value. The headache and muscular pains are relieved by aspirin, 1 to 2 grains, every two hours. Sodium salicylate in 2 grain doses every two hours may afford relief. For restlessness and insomnia, bromid of soda, 10 grains two or three times a day, or one allonal tablet night and morning will be of benefit. Small doses of Dover's powder, 1 to 5 grains according to age, will control the cough and ease the muscular pains. The nose and throat symptoms are relieved by local treatment.

Douching the nasal passages with hot normal salt solution is soothing and this can be followed by an oil spray, such as menthol, camphor, iodin, of each ½ grain, liquid albolene, 1 ounce. Instillation of a few drops of a 10 per cent solution of argyrol or silvol in the nose and eyes is recommended. Cold compresses around the throat or an ice-bag will often check the troublesome laryngeal cough. Steam inhalations of compound tincture of benzoin, 1 dram to a pint of boiling water, are very soothing. Antipyrin, 2 grains, bromid of soda, 5 grains, can be given internally every two hours until the patient is relieved. When the middle ear appears congested and is painful the use of the following ear drops, warmed and dropped in the ear every two hours, affords relief:

℞	Phenol	♏ij
	Liq. Epineph. Hydrochlor. (1:1,000).............	℥i
	Glycerin.	℥i

A paracentesis should be performed as soon as any bulging of the membrane occurs and the ear kept clean with a weak lysol solution, 5 drops to 5 ounces hot water.

The treatment of bronchitis and pneumonia does not differ from that caused by other organisms, the details of which treatment can be found in Volume IX of this series.

The treatment of the gastro-intestinal manifestations of influenza is symptomatic. In severe vomiting, fluids should be introduced by rectum or under the skin. When food is retained then gruels can be given first, followed by broths, boiled skimmed milk, etc.

The use of serum from convalescent patients has been recommended but is not necessary, except in the very severe cases with pulmonary involvement. Its use is still in the experimental stage.

The child is usually left in a weak and depressed condition after influenza, and general tonics—iron, strychnin, malt and cod-liver oil—may be used with advantage. The best tonics are nutritious food, plenty of sleep and rest, fresh air and sunlight.

PUBLIC HEALTH REGULATIONS

The Committee on the Control of Communicable Diseases of the American Public Health Association summarized our present knowledge of influenza as follows:

1. INFECTIOUS AGENT.—Undetermined.

2. SOURCE OF INFECTION.—Probably discharges from the mouth and nose of infected persons and articles freshly soiled with such discharges.

3. MODE OF TRANSMISSION.—Believed to be by direct contact, by droplet infection or by articles freshly soiled with discharges of the nose and throat of infected persons.

4. INCUBATION PERIOD.—Short, usually twenty-four to seventy-two hours.

5. PERIOD OF COMMUNICABILITY.—Undetermined, apparently during the febrile period or at least for seven days from onset of clinical symptoms.

6. METHODS OF CONTROL

(a) The infected individual and his environment

1. *Recognition of the Disease.*—By clinical symptoms only. Uncertain in interepidemic periods.

2. *Isolation.*—During acute stage of disease.

3. *Immunization.*—None; vaccines have not proved of definite value.

4. *Quarantine.*—None.

5. *Concurrent Disinfection.*—Discharges from the nose and throat of the patient.

6. *Terminal Disinfection.*—Airing and cleaning.

(b) General measures

During epidemics efforts should be made to reduce opportunities for direct-contact infection, as in crowded halls, stores, and street cars. Kissing, the use of common towels, glasses, eating utensils, or toilet articles should be avoided. The hands should be washed carefully before eating. In isolated towns and institutions, infection has been delayed and sometimes avoided by strict exclusion of visitors from already infected communities. The closing of schools has not been effective in checking the spread of infection. The use of masks by nurses and other attendants has proved of value in preventing infection in hospitals. Scrupulous cleanliness of dishes and utensils used in preparing and serving food in public eating places should be required, including the subjection of all such articles to disinfection in hot soapsuds. In groups which can be brought under daily professional inspection, the isolation of early and suspicious cases of respiratory tract inflammation, particularly when accompanied with a rise in temperature, may be relied upon to delay the spread of the disease. To minimize the severity of the disease and to reduce mortality, patients should go to bed at the beginning of an attack and not return to work without the approval of their physician.

CHAPTER XXIII

ACUTE RHEUMATIC FEVER

Definition.—Rheumatic fever is an infectious, non-contagious disease of undetermined origin, characterized by irregular fever, polyarthritis and in many cases inflammation of the cardiac tissues, especially the endocardium.

Synonyms.—Acute rheumatism, rheumatic fever; inflammatory rheumatism; polyarthritis rheumatica; acute articular rheumatism.

Epidemiology.—Rheumatic fever is a common disease. It occurs in practically all countries, especially in the temperate and subtropical zones. In Europe and America it constitutes from 3 to 7 per cent of medical cases admitted to the hospitals. It is not a reportable disease and is not a frequent cause of death, hence accurate statistics as to its incidence cannot be presented. It is important on account of its grave sequelæ and its tendency to recur.

Age.—Clinical experience shows that it is essentially a disease of the young and in general it may be stated that the younger the patient the greater the probability that he will be left a permanent cardiac cripple. It is most frequently observed in youth and early adult life. It is rare in infants, but children over five years of age are often attacked.

Other Factors.—*Sex* does not exert any influence upon the frequency of the disease. *Environment* and *occupation* which lead to exposure to cold and wet increase the liability to rheumatic fever. In some cases a single exposure to these conditions precipitates an attack. Chilling probably acts by lessening the resistance of the tissues to infection. Occasionally *traumatism,* by creating a *locus minoris resistentiæ,* determines the localization of the inflammation.

Seasonal Incidence.—The development of rheumatic fever seems to be especially favored by damp and changeable weather. In America the maximum number of cases is usually observed during the spring months, while in England the highest incidence is in the autumn. The prevalence and severity of rheumatism are subject to wide variations which are best explained on the ground of epidemic influence.

Etiology.—The resemblance of rheumatic fever to other acute infectious diseases indicates that a specific causative organism is responsible for the disease. A general septicemia is suggested by the clinical symptoms, *i.e.,* the

character of the fever, the arthritis, the tendency to relapse, the sweats, the anemia, and especially the involvement of the endocardium and the serous membranes. Newsholme has shown that rheumatic fever assumes a certain epidemic prevalence which occurs at intervals of three, four or six years with varying intensity and that a severe epidemic is followed by a period of low prevalence, further indication of its microbic origin. Although one may assume that a causative organism exists, its nature has not been determined. One group of observers has given the name of *Streptococcus rheumaticus* to organisms to which they assign certain characteristics, while the investigations of a larger group present satisfactory evidence that no such organism has been isolated. *Streptococcus viridans* may be grown on blood or joint fluids from the majority of cases of rheumatic fever. These organisms produce in rabbits certain lesions, *i.e.*, polyarthritis, tenosynovitis, endocarditis, pericarditis and pleurisy, which are identical with the lesions ascribed to the specific action of *Streptococcus rheumaticus*. Moreover, the same group of symptoms is obtained when strains of *Streptococcus viridans* from patients suffering from infections other than rheumatic fever are injected into rabbits. A biochemical and immunological classification of streptococci obtained from rheumatic fever patients shows that they do not fall into any distinctive group.

It has been suggested that the streptococci isolated from rheumatic fever patients may all be secondary invaders, as is the case with streptococci found in smallpox. Or possibly rheumatic fever is the peculiar response on the part of the patient to any one of several causative organisms rather than the specific effect of one. However, the specificity of the salicylates in rheumatic fever and their ineffectiveness in other types of streptococcic infection point to a single determining causative factor.

Birkhaug of Rochester isolated a non-methemoglobin-forming streptococcus from cases of acute rheumatic fever which he believes will prove to be the existing factor in the disease.

He found it in the tonsillar crypts in 96 per cent of cases of acute rheumatic fever and in the blood stream in 8 per cent.

From it he produced a toxin which when diluted 1:100 was used in forty-eight thousand children by Kaiser for intradermal tests similar to the Schick and Dick tests. Under three years of age, he obtained no reactions, and the greatest number of positive tests occurred between the ages of ten and fourteen years. In children in whom there had been a history of rheumatism, 72 per cent showed a positive reaction. This test, which is termed the Birkhaug test, shows the susceptibility of a child as does the Schick test for diphtheria and the Dick test for scarlet fever.

Pathology.—Cases of rheumatic fever which reach a fatal termination nearly all succumb as a result of an endocarditis rather than from the virus

of the infection. The serous membranes of the joints, pleura, and pericardium, the myocardium supplied by the branches of the coronary arteries and the large blood-vessels in the region of the vasa vasorum are the areas particularly affected by the action of the virus. Here a non-suppurative inflammation takes place which later goes on to the formation of connective-tissue scars.

The pathological changes in the joints are not striking. There is an increase in the amount of synovial fluid which becomes turbid and viscous and supplied with cellular elements. Upon standing, the fluid forms a dense network of fibrin.

In non-fatal cases the recovery is usually complete, so that no traces are left in the joints a few months after convalescence.

The subcutaneous nodules, characteristic of severe cases of the disease in children, show a central coagulation necrosis and a homogeneous transformation of the fibrils of connective tissue. The limits of the nodules are not sharply defined.

A serofibrinous inflammation follows the involvement of the pleura and pericardium. Recovery is by organization of the fibrin which, if extensive, leads to dense adhesions between the visceral and parietal layers.

The effect of the virus upon the endocardium is the formation of fine verrucæ upon the valves at the line of closure, upon the chordæ tendinæ and, more rarely, upon the mural endocardium. They result in the deformity of the valves and the attendant consequences.

The most characteristic lesion of the disease is in the form of the *Aschoff bodies* which lie in close connection with the blood-vessels of the myocardium. They are submiliary in size and are made up of various types of cells, the most characteristic of which is a giant-cell with many vesicular nuclei. They also contain polymorphonuclear leukocytes, lymphocytes, and plasma-cells. Healing is by the formation of scar tissue. Although bacteria have not been isolated from these *Aschoff bodies* it is a lesion found in no other disease, has never been induced by animal experimentation and is believed to be peculiar to rheumatic fever.

SYMPTOMS

Rheumatic fever, as seen in childhood, reveals its true nature as a general septicemia, dependent for its symptomatology upon the system involved. The polyarthritis which gives the characteristic group of symptoms in the adult may be comparatively unimportant in the child, even to the point of being overlooked. On the other hand, the tendency to cardiac involvement is tremendously increased. In the acute stage a rapid pulse and breathing, cardiac enlargement, and a systolic murmur at the apex may be the prominent symptoms. From 80 to 90 per cent of rheumatic fever patients under

ten years of age have cardiac involvement which may take the form of endo-
carditis, myocarditis, or pericarditis. These patients as a rule do not die
during the first attack but are left with a greater or less degree of permanent
injury. In some cases the endocarditis arises without any evidence of ar-
thritic involvement or in advance of such symptoms. It is also seen coinci-
dent with an attack of acute chorea. *Erythema nodosum* or *erythema
exudativum* sometimes accompany the endocarditis.

The symptoms of rheumatic fever are less acute in children than in adults
but act over a longer period and are often chronic in their manifestations.
The process is spread over many years with first one and then another group
of symptoms assuming prominence. Sometimes a mild persisting fever and
an increasing anemia may be the only symptoms. There may be only muscu-
lar aching, referred to as "growing pains."

The acute attack may be ushered in by prodromal symptoms, lasting from
a few hours to a day or two, which consist of general malaise, a sense of
fatigue, darting pains in the joints and a sore-throat. In many cases the on-
set is abrupt and marked by the simultaneous occurrence of chilliness, eleva-
tion of temperature and pain in one or more joints.

Arthritic Phenomena.—The classical appearance of the affected joint is
that of local inflammation with pain, swelling, redness, tenderness, and local
heat. The larger joints are the more frequently affected and those of the
lower extremities are attacked first. Those joints subjected to strain or ex-
posure to cold and wet are the first affected. The knees, ankles, shoulders,
and wrists are the more common sites of inflammation, but no joint is im-
mune and the hip and elbow joints and those of the hands and feet are often
included. A striking and characteristic feature is the migratory nature of
the arthritis which affects symmetrical joints simultaneously and leaves one
pair of joints as it affects another. It may attack the several joints in a
limb successively, *i.e.,* reaching the knees after the ankles. The same joint
may be affected two or three times before the infection is overcome.

The appearance is that of redness and swelling. The swelling is due to
edema of the soft parts as well as to effusion into the joint cavity. To pal-
pation it may be firm and elastic or soft and fluctuating, the latter being found
particularly in the large joints. In the knee the patella may be floating.

The redness, usually most distinct about the knees, elbows, ankles, and
wrists, is a diffuse blush which merges gradually into the normal color of
the surrounding skin. It is the first local sign to disappear and often may
not be present at all. The skin over the inflamed joint seems warmer to the
touch than upon other portions of the body. There is sometimes a disturb-
ance of the temperature sensation over the joints, some being unusually
sensitive to heat and others to cold.

The tenderness persists after the pain has left and seems to be located

chiefly in the soft parts. The pain is intense and is increased by the least motion. The patient lies motionless in bed, as every change in position results in intolerable pain. If many joints are involved he assumes a somewhat characteristic position of flexion of all joints. The Fowler position, *i.e.*, semirecumbent with the knees elevated by a pillow and the feet supported by a sandbag, is often the most comfortable. The weight of the bedclothes is frequently a burden. The pain is worse at night and the intensity seems to depend both upon the amount of effusion into the joints and the degree of swelling of the soft parts.

The duration of the acute process in a single joint varies from one to eight days, in some cases being prolonged to two weeks. The joints first involved are usually the first ones to clear up.

It is probable that the arthritis of rheumatic fever never goes on to suppuration unless there is a complicating infection. Those cases which respond to salicylates in a characteristic manner and yet show one or two joints suppurating are undoubtedly due to an invasion by some pyogenic organism.

Temperature.—The degree of fever, usually ranging from 101° to 104° F., corresponds with the severity of the arthritic symptoms. It is irregularly intermittent, is atypical and declines as a rule by lysis. *Prearthritic* fever may be the result of a prodromal angina or tonsillitis and may indicate the first localization of the infectious process on the heart valves or some other viscus. Such a course is comparatively frequent in children.

Febrile Remissions.—The temperature curve is the best guide to the progress of the disease. In the absence of new areas of inflammation the temperature shows a tendency to fall to normal, but with each new involvement or relapse of a joint or viscus there is an increase in the fever. Each climb of the temperature is a signal for a careful examination of the patient for endocarditis, pericarditis, myocarditis, pleurisy or pneumonia.

The duration of the fever is modified by treatment with the salicylates. The range is wide, with an average of between one and three weeks.

Hyperpyrexia occurs in a small proportion of patients. It is usually the cause of death in fatal cases at the acute stage. The disease may be running an ordinary course when in the second or third week the temperature rises rapidly to any point between 106° to 110° F. Cerebral symptoms occur simultaneously and the condition ends in coma and death. With the introduction of ice baths for the high temperature the mortality has been decreased.

Pulse.—In uncomplicated cases the pulse corresponds to the degree of fever. It may be full and bounding or dicrotic. Cardiac complications are reflected in the character of the pulse.

Respiration.—The respirations are usually increased in proportion to the degree of fever. Complications involving the lungs, pleura or pericardium increase the rate. Cardiac weakness is also registered in the rate and character of the respirations. Children, particularly those with cardiac complications, may breathe from 60 to 70 times per minute, entirely out of proportion to the temperature or pulse rate.

Perspiration.—Severe perspiration is a characteristic feature. It occurs most frequently at night and is so profuse as to soak the clothing. It often has a musty or sour odor. When the skin dries it is covered by a powdery crystalline deposit. Abundant sudamina accompany the sweating.

Subcutaneous Nodules.—When found, these are of distinct diagnostic and prognostic importance. They vary in size from a·millimeter to a centimeter in diameter. They occur in muscle and tendon sheaths, in the broad tendons as they pass over joints and over bony surfaces that are near the skin, and also in the subcutaneous tissues over the large muscles, where they differ from the others in that the skin over them is reddened. They are painless, are not accompanied by redness of the skin, except as noted above, and are freely movable except over bony surfaces. Ordinarily they are symmetrical in distribution and· appear in crops. When they appear as translucent spots they are detected only by careful palpation or sometimes by inspection of a flexed joint. They may last from a few weeks to several months.

Nodules are found·most frequently in children and only in severe cases. Most cases showing them have an accompanying endocarditis. Their appearance points to a grave prognosis.

Blood-Picture.—A moderate leukocytosis, from 12,000 to 20,000 is the rule. There is an increase in the polymorphonuclear neutrophils with each new joint involvement. *Anemia* is an outstanding feature of the disease. The number of red cells falls rapidly in the first two weeks of an acute attack with a corresponding or greater decrease in the hemoglobin. In children, especially, the anemia is manifested by a marked pallor, especially if there is an involvement of the pericardium.

Urine.—The urine is scanty, of a high specific gravity and very acid. It is rich in urates but deficient in chlorids. In cases running a high temperature there is a febrile albuminuria.

COMPLICATIONS

The response of the heart and its membranes to the virus of rheumatic fever may properly be considered a part of the symptomatology of the disease rather than as a complication. Particularly in children the cardiac manifestations are far more prominent than the arthritic ones. The cardiac phase

of rheumatic fever, however, is fully discussed in Volume XVI of this series and will not be repeated here. The treatment of cases of rheumatic fever with salicylates, which so effectively control the pain in the joints, does not guard against the cardiac involvement, and one may not assume that such danger is avoided when the patient becomes free from pain. A sudden rise in temperature and pulse rate which cannot be accounted for by the appearance of inflammation in a new joint or in the pleura is often the first evidence of endocarditis or myocarditis. The general symptoms are frequently of more diagnostic aid than heart murmurs which may be due to a relaxation of the cardiac ring as well as to verrucæ on the valves. Precordial pain is an important symptom of myocarditis. Enlargement of the area of cardiac dulness, change in the character of the heart sounds, rapid heart action and change in the character of the rate and rhythm are a part of the picture. Pericarditis is not accompanied by pain. Increase in temperature and pulse rate and the detection of a pericardial rub by careful auscultation indicate the onset of pericarditis.

Pleurisy.—Next to cardiac involvement the pleura is the large serous membrane most frequently affected by the rheumatic virus. This occurs usually in cases already having cardiac complications. The left side is more often involved than the right, or if both are involved the left shows the first signs. It is often a direct extension from one serous membrane to the other. As a complication of polyarthritis it begins in the second or third week of the disease by a sharp pain on inspiration. Signs of a simple fibrinous pleurisy are found upon examination, but in a day or two the signs change to those of pleural effusion. This persists for two to three weeks and the repair is by gradual absorption of the exudate. The general condition of the patient may indicate a pleuracentesis to relieve the strain upon the heart.

Pleurisy may occur as a late complication of arthritis or a precursor of it. It may begin as a dry pleurisy several weeks or months after the attack of arthritis. In these cases it often spreads rapidly and involves both the pleura and the pericardium. In children the absence of arthritis is often noted and an accompanying chorea may give the only hint as to the nature of the infecting virus. These acute attacks usually leave a crippled heart in their wake.

Pneumonia.—This is a severe complication which occurs during an acute attack. It usually does not appear except in company with other complications. Congestion of the lungs makes them an easy prey to secondary invaders which set up a true pneumonia with its characteristic symptoms.

Associated Conditions.—*Acute Chorea.*—While there is a general agreement that some relation exists between acute chorea and rheumatic fever, the nature of the relation remains unknown. Sometimes the two diseases occur together, but more frequently one precedes the other. It is sug-

gested that acute chorea is a cerebral manifestation, but this view is not generally accepted. It may be that the virus of rheumatism is one of the several cerebral irritants which produce chorea.

Acute Tonsillitis.—This often precedes or accompanies an attack of acute rheumatism. Here again the relation is obscure, but it is probable that the tonsil is one of the portals of entry of the inciting agent of rheumatic fever.

Cutaneous eruptions, especially erythema nodosum, erythema multiforme, and urticaria, sometimes develop during the course of rheumatic fever. Purpura may also appear, but there is no reason to believe that purpura rheumatica or Schönlein's disease is really the result of rheumatism.

DIAGNOSIS

Since the clinical picture of rheumatism in childhood differs from that seen in later life, its diagnosis in children is liable to be overlooked owing to the mildness of its symptoms and the absence of the typical polyarthritis seen in adults. The joint symptoms may be so slight that they are not detected or their significance is misinterpreted. Not uncommonly only one joint is involved. The slight pains are usually called growing pains and give the parents little concern until endocarditis or chorea appears. The heart is more liable to be involved in children and of those under ten years of age who have rheumatic fever from 80 to 90 per cent show evidence of cardiac involvement.

A history of tonsillitis frequently precedes an attack of acute rheumatic fever. The subcutaneous nodules should be searched for in every case, as they have great diagnostic importance. They can be more easily palpated if the forearm or leg is tightly flexed.

Differential Diagnosis.—For all practical purposes acute rheumatism can be excluded in infants under two years of age. Infantile scurvy with enlarged joints due to hemorrhages and the great hyperesthesia is sometimes diagnosed as rheumatism, but the spongy and discolored gums and the rapid improvement following the use of fruit juices should clear up the diagnosis.

Multiple gonorrheal arthritis has often been diagnosed as rheumatism, but the examination of the discharges will reveal the true condition.

Cases of general sepsis may be accompanied by joint pains resembling rheumatism.

Syphilitic arthritis develops more slowly without temperature and the presence of a positive Wassermann proves the diagnosis.

Arthritis may follow various infectious diseases, notably scarlet fever. This may appear as a simple arthritis or a purulent polyarthritis, and either may be complicated with an endocarditis. The previous history of the infectious disease will indicate the diagnosis.

Still's disease is a slow, progressive inflammation with enlargement of the joints, usually multiple, affecting the knees, wrists, and fingers. Salicylates will promptly relieve the joint pains of rheumatic fever, but have slight or no effect on arthritis due to other causes.

Prognosis.—Age is an important factor in the prognosis. There is little or no damage to life from an attack of acute rheumatic fever itself as long as the heart is not involved. This organ is chiefly affected in the first decade of life, this being the period also when the mortality is highest. The little patient rarely succumbs to the first attack, but the great danger lies in the reinfections or relapses. Much depends on the treatment during and after the attack. Rest in bed for several weeks thereafter and the use of salicylates reduce the chances of a severe endocarditis. Reinfection can be lessened by the removal of the tonsils, carious teeth or other foci of infection. Change to a warm equable climate is of decided advantage. A child who has once suffered from an attack of rheumatism is more liable to reinfections, and everything possible must be done to keep him in the best possible condition and under constant supervision.

TREATMENT

Prophylaxis.—Every effort should be made to prevent subsequent attacks of rheumatism. Exposure to cold, dampness or living in poorly ventilated houses amidst unsanitary surroundings must be avoided. A slight exposure, such as would have little effect on a normal child, might start an attack in a child who has had the disease. This does not mean that the child must live in a glass house and be a hothouse plant. Abundant opportunity must be given for outdoor exercise and fresh air. When circumstances warrant, a child subject to rheumatism should be removed to a warm dry climate.

There is no doubt that enlarged and diseased tonsils play some part in the development of this disease and their removal is indicated in order to do away with a source of infection as well as a possible portal of entry. At the same time the adenoids should be removed. The operation is best done between attacks. While a complete tonsillectomy does not insure freedom from consequent attacks, yet the removal of diseased tonsils improves the child's general condition and renders him more resistant to infection.

General Treatment.—The objects to be attained are comfort, relief of pain, and prevention of heart complications. The most important means of obtaining them is rest. The child must be put to bed and kept in bed. For his comfort the bed should be raised by a good soft, smooth mattress and the patient protected with light but warm covering and kept in a large, airy room. He must remain in this bed for five or six weeks even after the

fever and acute symptoms have subsided. Such rest reduces the blood-pressure, lowers the pulse rate, and lessens the danger of heart complications and also gives relief to the joint and muscular pain. If the joints are inflamed they should be immobilized either by splints, pillows, or sandbags. The pain can often be relieved by hot compresses, or from cold applications if these give greater relief. Gently rubbing with some oil or lubricant oils containing salicylates, such as oil of wintergreen or mesotan, acts as a mild counterirritant and affords a means of absorbing salicylates. After rubbing, the joints should be wrapped in absorbent cotton.

When there is much sweating the body can be sponged with alcohol, dried with a soft towel and talcum powder freely applied. Flannel pajamas are preferable to cotton or linen.

Since the bodily strength is drained by a prolonged fever, the diet should be as liberal as possible, a lesson learned from the study of proper diets in typhoid fever cases. That meats and acids are harmful is an old superstition that it is hard to overcome, but during the acute stage overfeeding and overtaxing the digestive system must be avoided as in all acute febrile diseases. Milk should be given freely. Cereals can be cooked in milk, and eggs are not contra-indicated. Plenty of fruits should be given and also fruit juices, lemonade and alkaline mineral waters. It is a wise plan with children never to give the medicine at the same time as the feeding and never to introduce it into the food, for this associates in the mind of a child the taking of medicine with the taking of food, which is bad psychology.

The use of salicylic acid and its derivatives in rheumatism is considered by many as specific as the use of quinin in malaria. The salicylates do relieve the pains, reduce the fever, allay the joint inflammation and possibly shorten the attack. To obtain the best results care must be taken in its administration. In overdoses and when the body tolerance is reached it will produce characteristic symptoms. These are ringing or buzzing in the ears, nausea and vomiting, cardiac arhythmia, disturbances of vision and even delirium.

Salicylic acid is not borne well by children. Sodium salicylate well diluted in water is most generally used. A child five years of age should take from 30 to 60 grains a day in divided doses.

Alkalines, such as bicarbonate of soda, should be given in at least twice the dose of the salicylates, as they help to prevent any gastric irritation.

Aspirin and novaspirin are well borne by children, while tolysin has the great advantage of being tasteless and more easily administered to young children.

If the pain is intense it may be necessary to give—temporarily—morphin or codein. Allonal is a useful preparation to ease the pain and to produce sleep.

Vaccines and sera have been recommended, but the consensus is that their use has not yielded results which warrant a recommendation of the method.

The treatment of the cardiac complications can be found discussed in the volume on circulatory diseases of this series.

Proper care during the period of convalescence is most important. Emphasis has already been laid on the necessity for rest, especially in cases which show signs of cardiac involvement. It should be borne in mind that signs of valvular heart disease may not appear for weeks after the acute disease, so our little patients must be watched for a long period. The tendency to relapse must be guarded against and very great care taken to improve the general health and strength.

Anemia is a frequent complication and is best treated with iron in the form of the carbonate or citrate and combined with $\frac{1}{200}$ grain of arsenious acid or two drops of Fowler's solution. Including liver in the diet has a marked effect.

CHAPTER XXIV

ERYSIPELAS

Definition.—Erysipelas is an acute inflammation of the skin and mucous membranes caused by a hemolytic streptococcus. The disease is accompanied by fever, constitutional symptoms and a characteristic erythematous rash. It is communicable in that abrasions of the skin and mucous membranes are susceptible to infection by contact with cases or carriers.

Synonyms.—Erysipèle; Rothlauf; risipola.

History.—St. Anthony's Fire, as it used to be popularly called, dates back to antiquity. Hippocrates wrote a detailed description of erysipelas in his book on *Epidemic Diseases* and many of the writers of the early centuries described this disease. Heberden in 1807, in his *Epitome of the Diseases of Children* as quoted by John Ruhräh, gave the following description of erysipelas in children: "A disease bearing some affinity to the erysipelas sometimes attacks children in the first month, especially those who are born in public hospitals. . . . Wherever it is formed the skin becomes hard and livid; there is not much swelling, but the parts which are affected by it have a tendency to gangrene, especially the scrotum in boys. . . . It often proves fatal in a few days."

Rousseau called attention to the relationship between puerperal infections of the mother and erysipelas in the newborn. Fehleisen in 1882 was the first observer to demonstrate the rôle of streptococci in producing the disease. Tunnicliff in 1920 showed that *Streptococcus erysipelatis* of the group of hemolytic streptococci was the causative organism.

Etiology.—This disease sometimes appears in epidemics which are generally limited to the wards of hospitals or institutions. Such outbreaks were frequent in the early part of the eighteenth century when the cause of the infection was unknown, hospitals were overcrowded, and the importance of asepsis and antisepsis not known. Climate seems to have no influence on the frequency of the disease and there does not appear to be any racial immunity, but girls are not so frequently affected as boys.

A run-down condition, anemia, malnutrition or any factor that tends to lower the body resistance are predisposing influences. The infection may start from the site of a wound, fissure, or abrasion which may be so small as not to be visible to the naked eye. The germ may be carried by direct contact, unwashed hands, soiled towels, unclean instruments, etc. Vaccina-

tion wounds and ears pierced for earrings have been sites of the infection. In newborn infants the process usually starts about the umbilicus and is the result of faulty technic or carelessness on the part of the physician or attendant, particularly in the care of the cord. Circumcision wounds may become the portal of entry for the streptococci.

The *Streptococcus hemolyticus* is the active cause of the disease. It occurs in short snakelike chains and is not decolorized by Gram's method. It ferments dextrose, lactose and saccharose, but not mannite. It may retain its virulence for months in dried blood, pus, or in dust of rooms. Septic cases, especially those of the nose, throat, and ears frequently start outbreaks in medical wards.

Symptoms.—The incubation period is short, averaging about three days. When the disease occurs in the newborn it is called *erysipelas neonatorum* and appears from three to seven days after birth. While erysipelas in infants usually starts from an umbilical infection, it may follow a circumcision or abrasions from forceps. Fortunately it is not nearly so frequent now that greater care and cleanliness are employed in obstetrics, a case of this kind being looked upon as a reflection on the skill of the doctor or nurse.

The first symptoms are high temperature, convulsions, prostration and refusal to nurse. The inflammation spreads over the abdomen or to the peritoneum, the pleura and even to the liver, where it may cause a hepatitis accompanied with icterus. Abscesses are liable to form and gangrene may be a result. The mortality is very high in infants, death following a convulsion or extension of the disease to other organs. This condition is more fully described in Volume III of this series.

In older children the first symptom is usually a chill followed by high fever. This is often accompanied by soreness of the throat and redness at the point of entry. The site of the infection is red and swollen and tender on pressure; the lesion has a sharp border and feels hard and stiff, while the skin has a shiny surface and a distinct red color. The disease spreads by irregular advances at the edge and is often checked where the skin is closely adherent to deeper structures. The swelling is more marked and edematous where the tissue is loose. The skin may become vesicular or may suppurate. Gangrene is a complication seen more often in young children than adults. The scalp is frequently involved and the entire face may be so swollen as to be unrecognizable in children. The adjoining lymph-nodes are usually enlarged. Fever is present as long as the skin lesion spreads; it may reach 104° F. or even higher and may continue in a remittent or intermittent manner. During the febrile period the symptoms of sepsis are present, such as drowsiness, malaise, and loss of appetite. The absence of acute pain is characteristic. There is a burning sensation of the skin as well as a stiffness of the muscles.

Complications.—The most frequent complications associated with erysipelas are abscesses and suppuration under the skin. Extensive areas of pus develop which give a soft, baggy sensation on pressure. There is very little tenderness. The skin about the eyes may become so thickened and edematous as to almost close the orbital slit. The hair often falls out in cases where the scalp is involved.

Albuminuria is not uncommon during the height of the infection, but permanent kidney disease is rare.

In young infants gangrene or pertitonitis are very dangerous complications.

Diagnosis.—There is usually no difficulty in making a diagnosis after the characteristic skin lesion appears. The advancing margin of infiltration and redness with the sharp line of demarcation and constitutional symptoms associated with the fever are not found in any other skin infection. Acute eczema is usually accompanied by itching with some oozing and no sharp line of demarcation.

Before the skin lesion appears the picture is that of some general infection.

Prognosis.—In young infants the mortality is very high. If the causative streptococci are present in the blood the prognosis is much worse than when the blood is sterile. Some observers claim that a high leukocytosis, over 25,000, is an unfavorable sign. The outcome is more serious if the mucous membranes are involved. When there is a gradual fall in the number of leukocytes the prognosis is better than when there is a rise.

Treatment.—*Prophylaxis.*—Erysipelas in the newborn at least is a preventable disease. Cleanliness must be observed in everything concerned with the care of the baby. Direct or indirect contact with septic or suppurative cases must be avoided. The newborn baby must be protected from persons suffering from colds. If a case of erysipelas occurs in a hospital the baby must be isolated and the nurses or attendants not be allowed to go near other infants.

Medicinal.—There is no specific internal remedy for this disease. Some favorable reports have followed the use of a monovalent antistreptococcus serum prepared from the *Streptococcus erysipelatis*. Vaccines have been used but without benefit. The use of blood-serum from convalescent and recovered cases has been advocated, but there have not been enough cases so treated to allow for the formation of any definite opinion.

Birkhaug of Rochester has obtained a serum prepared from the blood of immunized horses which has given excellent results in a large number of cases. To obtain the best results, large doses, 25 to 50 c.c., of the concentrated serum must be used. Cases in which this antitoxin is used clear up very rapidly.

Early blood transfusion has proved of value in infants with *Streptococcus neonatorum*.

All sorts of local applications and treatments have been tried and each has its advocates. Ichthyol is perhaps the most widely used. It has the advantage of being astringent in its action as well as antiseptic. It may be painted over the affected area in a 25 per cent solution or combined with lanolin, three parts to one part of ichthyol, or with collodion in the same strength. Some prefer compresses of a saturated solution of magnesium sulphate. Ice compresses are of benefit in some cases, while great relief and therapeutic action are obtained from hot boracic acid packs. The use of ultra-violet rays has brought about a rapid cure, according to some reports. The general hygienic care is important and an experienced nurse is a great factor in bringing about a cure. The food should be of sufficient caloric value—milk, cereals, eggs, etc.

Stimulants are often indicated and whisky in large doses is of decided value. For sleeplessness one allonal tablet every six hours for a young child will give much comfort.

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