been corrected. I am sure that many of the cases sent into the health offices as cerebro-spinal fever are instances of the cerebral form of typhoid.

I have already referred to the fact that the malignant form of small-pox may be mistaken for cerebro-spinal meningitis.

It could scarcely be possible to confound tetanus with this disease.

Prognosis.—Hirsch states that the mortality has ranged in various epidemics from 20 to 75 per cent. In children the death-rate is much higher than in adults. Cases with deep coma, repeated convulsions, and high fever rarely recover. The outlook in the protracted cases is not good, though Heubner gives an instance of a lad of seven, who was ill from the end of February until the end of June, with repeated recurrences, was worn to a skeleton, and yet completely recovered.

Treatment.—The high rate of mortality which has existed in most epidemics indicates the futility of the various therapeutical agents which have been recommended. When we consider the nature of the local disease and the fact that, so far as we know, simple or tuberculous cerebro-spinal meningitis is invariably fatal, we may wonder rather that recovery follows in any well-developed case.

In strong robust patients the local abstraction of blood by wet cups on the nape of the neck relieves the pain. General bloodletting is rarely indicated. Cold to the head and spine, which was used in the first epidemics by New England physicians, is of great service. A bladder of ice to the head, or an ice-cap, and the spinal ice-bag may be continuously employed. The latter is very beneficial. Judging from the beneficial effects of the general bath in typhoid with pronounced cerebro-spinal symptoms, hydrotherapy should be systematically employed if the temperature is above 102½°. In private practice the cold-pack or sponging may be substituted. If any counter-irritation is thought necessary, the skin of the back of the neck may be lightly touched with the Paquelin thermo-cautery. Blisters, which have been used so much, are of doubtful benefit and should not be employed. Of internal remedies opium may be given freely, best as morphia hypodermically. Stillé recommends either a grain of opium every hour in severe cases or every two hours in cases of moderate severity; von Ziemssen advises the hypodermic of morphia, from one third to one half grain in adults. Mercury has no special influence on meningeal inflammation. Iodide of potassium is warmly recommended by some writers. Quinine in large doses, ergot, belladonna and Calabar bean have had advocates. Bromide of potassium may be employed in the milder cases, but it is not so useful as morphia to control the spasms.

The diet should be nutritious, consisting of milk and strong broths while the fever persists. Many cases are very difficult to feed, and Heubner recommends forced alimentation with the stomach-tube. These cases seem to bear stimulants well, and whisky or brandy may be given freely when there are signs of a failing heart.

XV. DIPHTHERIA.

Definition.—A specific infectious disease, characterized by a local fibrinous exudate, usually upon a mucous membrane, and by constitutional symptoms of varying intensity. The presence of the Klebs-Loeffler bacillus may be regarded as the etiological criterion by which true diphtheria may be distinguished from other forms of pseudo-membranous inflammation.

Historical Note.—The disease was known to Aretæus and Galen. Epidemics occurred throughout the middle ages. It appeared early among the settlers of New England, and accounts are extant of epidemics in this country in the seventeenth and eighteenth centuries. Huxham and Fothergill gave excellent descriptions of the disease. An admirable account was given by Samuel Bard,* of New York, in 1770, whose essay is one of the most solid contributions made to medicine in America. It was reserved for Pierre Bretonneau, of Tours, to grasp the fact that *angina suffocativa*, "*cynanche maligna*," the "putrid" and other forms of malignant sore throat were one and the same disease, to which he gave the name "diphthérite."

Etiology.—The disease is endemic in the larger centres of population, and becomes epidemic at certain seasons of the year. It is a remarkable fact that while other contagious diseases have diminished within the past decade, diphtheria, particularly in cities, has increased. It is by no means confined to the poorer districts, but occurs in the houses of the better classes, particularly when the plumbing is defective. The disease is, however, not confined to cities. It has prevailed with great severity in country districts, in which indeed the affection seems to be specially virulent. The relation between imperfect drainage and the diphtheria poison has not yet been satisfactorily determined. Perhaps, as Thorne suggests, the faulty conditions produce sore throat of a benign character, which, as in scarlet fever, affords a soil suitable for inoculation by the diphtheria germ, when present in the air. Drains, too, he thinks may retain the virus received through the sputa and dejecta of the sick. This author states that no prevalence of diphtheria has ever been definitely traced to polluted water.

Diphtheria is a highly contagious disease, readily communicated from person to person. The poison is given off in the pharyngeal secretion and in the saliva, but not in the breath. No disease of temperate regions proves more fatal to physicians and nurses. There seems to be particular danger in the examination and swabbing of the throat, for in the gagging, coughing, and spluttering efforts the patient may cough mucus and flakes of membrane into the physician's face. The virus attaches itself to the clothing, the bedding, and the room in which the patient has lived, and

* Transactions of the American Philosophical Society, vol. i, Philadelphia, 1770.

has, in many instances, displayed great tenacity. The disease may be transmitted by inoculation. The contagion does not seem to be widely diffused in the neighborhood of the patient. At the Montreal General Hospital we rarely had cases develop in the wards adjacent to those in which there were diphtheria patients.

There is a wide-spread belief in the profession that the disease may be communicated from animals. There is in calves a contagious pseudo-membranous affection which is said to be communicable to man. Cows are not known to be affected spontaneously. In the epidemics in which the contagion has been traced to the milk, it is more probable that the virus has been accidentally mixed with it than that the cows were themselves diseased. Cats are subject to a pseudo-membranous disease, and there are many cases on record in which children appear to have caught diphtheria from them. On the other hand, I know of one case in which a cat died of angina and intense pseudo-membranous colitis, and the children who nursed it did not take the disease; and of a second case, in which a pet cat had coryza, difficult breathing, fever, and enlarged cervical glands, and here too the children were not affected. The so-called diphtheria of fowls is apparently not associated with the same germ as the human diphtheria.

Of predisposing causes *age* is one of the most important. Very young children are rarely attacked, but Jacobi states that he has seen three instances of the disease in the newly born. Between the third and the fifteenth year a large majority of the cases occur. In this period the greatest number of deaths is between the second and the fifth years. Girls are attacked in larger numbers than boys, probably because they are brought into closer contact with the sick. Adults are frequently affected. The disease is most prevalent in the cold autumn weather.

Caillé regards as special predisposing elements in children, enlarged tonsils, chronic naso-pharyngeal catarrh, carious teeth, and an unhealthy condition of the mucous membrane of the mouth and throat.

Epidemics vary in intensity. While in some the affection is mild and rarely fatal, in others it is characterized by wide extension of the membrane, and shows a special tendency to attack the larynx.

The Specific Germ.—The bacillus originally described by Klebs and more thoroughly studied by Loeffler appears to be the specific virus. It is found in the pseudo-membranes, not in the subjacent mucosa, or in the blood, or in the internal organs. It is a non-motile bacillus, varying from 2·5 to 3 μ in length, and from 0·5 to 0·8 μ in thickness. It appears as a straight or slightly bent rod with rounded ends. Irregular bizarre forms, such as rods with one or both ends swollen, are, however, not uncommon. The bacillus stains in sections or cover-glass specimens by Gram's method. It is best cultivated on blood serum and bouillon. The colonies are large, elevated, grayish-white, with an opaque centre. Welch and Abbott also state that it grows well on potato; but the growth is invisible or indicated

only by a dry thin glaze. It multiplies readily in milk. Although it forms no spores, it is a very persistent bacillus, and cultures have been made from membrane preserved for five months in a dry cloth. The cultures inoculated into the trachea of animals produce a well-marked diphtheritic exudation with development of the bacilli and secondary involvement of the lymph-glands, in which remarkable necrotic areas occur, with fragmentation of the nuclei (Flexner). Brieger and Fränkel have separated from the cultures a tox-albumin, which, injected into animals, produces paralysis, nephritis, and albuminuria. This point tends strongly to confirm the view that this bacillus is really the infective agent in the disease. It is one of the most virulent poisons known, and when injected in a sufficiently small though fatal dose, there may be no symptoms for days, and the animal may not develop the paralysis for weeks or even months after the injection. A point of very great interest is the fact that cultures from cases vary in virulence, and this is in accord with the remarkable variation in the intensity of different epidemics and different cases. As a rule there is a correspondence between the virulence of the bacilli and the gravity of the case.

Associated with the Klebs-Loeffler bacillus are other pathogenic bacteria, which probably play an important *rôle* in the complications of the disease. Thus streptococci and staphylococci are frequently present in the exudate, and to their invasion through the abraded mucosa are due the secondary suppurations and inflammations of serous surfaces, and to the aspiration of the streptococci into the lungs the common and fatal broncho-pneumonia.

Diphtheria may then be said to be caused by the Klebs-Loeffler bacillus. The production of a false membrane is the local or primary effect; the constitutional symptoms are due to the absorption of the poison in varying doses, while the secondary inflammations are associated with the invasion of the ubiquitous pus organisms.

Pseudo-diphtheritic Processes.—Many substances have the power of exciting pseudo-membranous or croupous inflammation, the exudate of which is not distinguishable from that of diphtheria. Some of them are non-microbic, as steam, ammonia, and chlorine; others are dependent upon micro-organisms, and must be distinguished from true diphtheria.

(*a*) There are cases of pseudo-membranous angina, associated with which is a bacillus identical, morphologically and in its behavior on culture media, with the Klebs-Loeffler bacillus, but which is not pathogenic—i. e., does not produce the tox-albumin, and is harmless when inoculated. Whether this is an attenuated form, as Roux and Yersin hold, is not yet settled. This complicates the question of diagnosis. A patient in my ward presented a thin, grayish pseudo-membrane over the tonsils and fauces, without fever and without constitutional disturbance. Non-pathogenic bacilli, identical with those of true diphtheria, were found by Welch

and Abbott. We need additional information upon the occurrence of this form and its relation to the virulent bacillus.

(*b*) The pseudo-membranous angina of the eruptive fevers is an affection distinct, etiologically at least, from true diphtheria. In a majority of all these cases, particularly in scarlet fever, the Klebs-Loeffler bacillus is absent, and this is in accord with the fact that scarlatinal angina rarely communicates diphtheria, and is still more rarely followed by paralysis.

Streptococci and staphylococci are present in the membranes in these cases. Late in the disease infection with the *bacillus diphtheriæ* may occur, and it is probable that under these circumstances alone is the angina followed by symptoms of paralysis.

Morbid Anatomy.—A majority of the cases die of the faucial or of the laryngeal disease. The exudation may occur in the mouth and cover the inner surfaces of the cheeks; it may even extend beyond the lips on to the skin. This was met once in thirty autopsies at the Montreal General Hospital. The amount of exudation varies in different cases. Usually the tonsils and the pillars of the fauces are swollen and covered with the false membrane. More commonly, in the fatal cases, the exudation is very extensive, involving the uvula, the soft palate, the posterior nares, and the lateral and posterior walls of the pharynx. These parts are covered with a dense pseudo-membrane, in places firmly adherent, in others beginning to separate. In extreme cases the necrosis is advanced and there is a gangrenous condition of the parts. The membrane is of a dirty-greenish or gray color, and the tonsils and palate may be in a state of necrotic sloughing. The erosion may be deep enough in the tonsils to open the carotid artery, or a false aneurism may be produced in the deep tissues of the neck. The nose may be completely blocked by the false membrane, which may also extend into the conjunctivæ and through the Eustachian tubes into the middle ear. In cases of laryngeal diphtheria the exudate in the pharynx may be extensive. In many cases, however, it is slight upon the tonsils and fauces and abundant upon the epiglottis and the larynx, which may be completely occluded by false membrane. In severe cases the exudate extends into the trachea and to the bronchi of the third or fourth dimension. This occurred in nearly half of my thirty Montreal autopsies.

In all these situations the membrane varies very much in consistency, depending greatly upon the stage at which death has occurred. If death has occurred early, it is firm and closely adherent; if late, it is soft, shreddy, and readily detached. When firmly adherent it is torn off with difficulty and leaves an abraded mucosa. In the most extreme cases, in which there is extensive necrosis, the parts look gangrenous. In fatal cases the lymphatic glands of the neck are enlarged and there is a general infiltration of the tissues with serum; the salivary glands, too, may be swollen. In rare instances the membrane extends to the gullet and stomach.

Histological Changes.—We owe largely to the labors of Wagner, Weigert, and more particularly to the splendid work of Oertel, our knowledge of the minute changes which take place in diphtheria. The following is a brief abstract of the views of the last-named author:

The diphtheritic poison induces first a necrosis or death of cells with which it comes in contact, particularly the superficial epithelium and the leucocytes. The deeper cells of the mucosa and of the other parts reached by the poison may also be affected. The second change is hyaline transformation of the dead cells, or, as Weigert terms it, the production of coagulation-necrosis. The bacilli excite inflammation with the migration of leucocytes, which are destroyed by the poison and undergo the hyaline change. The superficial epithelial layers undergo a similar alteration, and what we know as the false membrane represents an aggregation of dead cells, most of which have undergone the transformation into hyaline material. This is in all probability a conservative process by which, in a measure, the poison is localized and prevented from reaching the deeper structures. The laminated condition of the exudate is probably produced by the inflammation of different layers. The formation of these foci of necrobiosis, starting from the epithelium and proceeding inward, is, according to Oertel, the distinguishing characteristic of diphtheria. The action of the poison is by no means confined to the superficial mucosa on which the bacilli grow. Although they do not themselves penetrate deeply, the contiguous bronchial glands show extensive foci of necrosis. In severe cases these necrotic areas are found in the internal organs, in the solitary glands of the intestines, and in the mesenteric glands.

The blood-vessels may themselves be much altered and the capillaries may show extensive hyaline degeneration. Every one of the histological changes described by Oertel in human diphtheria may be paralleled in the experimental disease induced by the Klebs-Loeffler bacillus, particularly the necrotic areas in the deep-seated organs, associated in the lymph-glands with a remarkable fragmentation of the nuclei.

The changes in the *other organs* are variable. When death has occurred from asphyxia there is general congestion of the viscera.

Capillary bronchitis, areas of collapse, and patches of broncho-pneumonia are almost constantly found in fatal cases. In very malignant cases the blood may be fluid. Fibrinous coagula may be found in the heart, but the wide-spread idea that they may cause sudden death is erroneous. Myocardial changes are not infrequent, and in certain cases sudden death is due to heart-failure in consequence of degeneration of the muscle-fibres. Endocarditis is extremely rare. It was not present in one of my thirty autopsies. The serous membranes often show ecchymoses. The kidneys present parenchymatous changes, such as are associated with acute febrile affections. There may, however, be acute nephritis. The spleen and liver show the usual febrile changes. The spleen is, however, not always enlarged.

Symptoms.—The period of incubation varies. In the cases of acci-

dental inoculation the duration is from two to three days. In cases in which the disease is contracted in the usual way it is from seven to twelve days. The initial symptoms are those of an ordinary febrile attack: slight chilliness, fever, and aching pains in the back and limbs. In mild cases these symptoms are trifling, and the child may not feel ill enough to go to bed. Usually the temperature rises to 103° or even more. There may be convulsions at the outset. In an attack of ordinary severity there is at first redness of the fauces, and the child complains of slight difficulty in swallowing. The exudate first appears upon the tonsils. It may be difficult to distinguish the patchy diphtheritic pellicle from the exudate in the tonsillar crypts. The swelling of the throat increases and the glands of the neck become involved. Usually by the third day the membrane has covered the tonsils, and crept on to the pillars of the fauces, and even to the uvula, which is now thickened and œdematous and completely fills the space between the swollen tonsils. The false membrane may extend also to the posterior wall of the pharynx. At first grayish white in color, it changes to a dirty gray, often a yellowish gray. The membrane is firmly adherent, and if removed leaves a bleeding, somewhat eroded surface. New membrane rapidly forms in place of that removed. The general condition of the patient, in a case of moderate severity, is fairly good. The temperature is not necessarily high, and in the absence of complications the range is from 102° to 103°.

At this stage, say the fourth or fifth day of the disease, the condition of the child is favorable. The pulse and temperature are not much above 100°; the throat symptoms are not of extreme severity; and the constitutional depression is not extreme. The symptoms may then abate and the swelling of the neck diminish. The false membrane separates, and by the eighth or tenth day the throat is clear and convalescence begins.

Deviations from this favorable course result either from extension of the local disease or from systemic infection.

(1) **Extension.**—The inflammation may pass into the posterior nares, obstructing the respiration, causing a very acrid and fœtid discharge, and usually a marked aggravation of the constitutional symptoms. The glandular inflammation is usually more intense; due, as Jacobi points out, to the greater richness of the nasal mucosa in lymphatics, which thus favors systemic infection. Though usually secondary, nasal diphtheria may be primary. It greatly increases the danger in any case. From the nose the inflammation may extend through the tear-ducts to the conjunctivæ and into the antra. In these cases the disease is more apt to involve the ears, through the Eustachian tubes, causing otitis media and perforation of the drum.

Extension of the inflammation downward into the larynx is by far the most serious complication of the disease. It is particularly dangerous in children, because it produces what is known as diphtheritic croup. The symptoms are identical with those of ordinary membranous croup.

In many instances the pharynx is but slightly involved. There may be only a trifling patch upon one tonsil. The first symptoms of laryngeal affection are huskiness of the voice, a brazen cough, and stridulous, noisy inspiration and expiration. With increasing obstruction the respiration becomes greatly embarrassed, the lower thoracic zone and the lower sternum are drawn in with each inspiration, and the supra-clavicular and intercostal spaces are depressed. Too often there is a gradually deepening cyanosis, and the child dies asphyxiated.

The exudation may extend into the trachea and bronchi, which become lined by a uniform sheeting of false membrane. It is not always easy to say, during life, whether exudation has taken place into these parts. In the performance of tracheotomy, when membrane is found in the trachea the outlook is generally bad. Occasionally the tracheal and bronchial membrane is coughed up as a definite mould.

(2) **Systemic Infection.**—In mild cases of diphtheria the constitutional disturbance is very slight. There may even be extensive local disease without great constitutional disturbance. As a rule, however, the general symptoms bear a definite proportion to the severity of the local disease. There are rare instances in which from the outset, even before the pharyngeal symptoms are at all well-marked, the constitutional prostration is extreme, the pulse frequent and small, the fever high, the nervous phenomena are pronounced; and the patient sinks in two or three days, overwhelmed by the severity of the poison. In some of these cases the exudation is chiefly nasal; in others the exudation is marked, but the throat symptoms are by no means extensive. It is specially to be noted that the temperature may not be raised; it may even be subnormal. The malignant diphtheria of this kind is fortunately rare. The severe systemic symptoms appear more commonly at a later date, when the pharyngeal symptoms are at their height. They are invariably met when the disease is extensive and when there is a sloughing fœtid condition in the pharynx causing an offensive odor of the breath. The lymphatic glands are greatly enlarged; the pallor is extreme, the color of the face an ashen gray, the pulse is rapid and feeble, and the temperature sinks below normal. In the most aggravated form there are gangrenous processes in the throat. If life is prolonged there may even be extensive sloughing in the tissues of the neck.

There are, of course, many variations in the above clinical picture. The cases may be so mild as scarcely to be recognized. Such cases, indeed, are often mistaken for ordinary lacunar tonsillitis. There are also certain anomalous forms which may be mentioned; cases which come on insidiously, with a tonsillitis of so mild a grade that it may be overlooked, and which is followed by a diphtheritic croup or a severe broncho-pneumonia. In rare instances the disease may almost be termed chronic, since the membrane remains upon the tonsils and pharynx for weeks.