

has wholly confirmed this opinion. On the other hand, contaminated objects that have been packed up and kept shut out from the air retain their virulence for a greater or less length of time, as may be shown by many instances.

Seventh, Can cholera be transported by merchandise? Although merchandise imported from India, whether to Suez or directly to Europe, has never been known to transmit cholera, this method of transportation is not absolutely impossible, and many of the materials brought from India—cloths, and so on—retain in their interstices a confined air that certainly might preserve and transport for a great distance the contagion with which they may be impregnated; but although this is a possibility, it is not probable, and the conference of Constantinople unanimously accepted the absence of proofs of the transportation of cholera by merchandise, while it admitted the possibility of its being done, under certain conditions. Since that time, Zehnder, the Swiss delegate to the Vienna Conference, in 1874, cited facts in favor of the danger of rags in transporting contagion (see the report of the International Sanitary Conference of 1874, page 272). But at the conference in Rome, in 1885, Koch disputed the interpretation that had been put upon these facts.

Eighth, water is perhaps the most important agent in the spread of cholera, and evidence to this effect was obtained long before the discovery of the cholera spirilla. J. Simon brought out some facts in England which confirm this statement. At London thirteen deaths out of a thousand inhabitants occurred among those whose houses were supplied with river water in the neighborhood of the sewer. Tested at this point, the water yielded forty-six grains of solid residue to the gallon. In other houses in the city that were in the same hygienic condition, but not supplied with this water, the mortality was only three and seven-tenths in a thousand, but the water which they used had been taken from outside the city, and yielded only thirteen grains of solid residue to the gallon.

It is not improbable that the cholera vibrio can live longer in a pure water than in one containing large numbers of other micro-organisms. It has remained viable for eight hundred and seventy-eight days in a sterilized pond water, which for at least three hundred and five days contained other bacteria. During this period they retained their usual susceptibility to heat and desiccation, showing that a true spore formation of the usual kind is not necessary for prolonged viability in this species.

At Halle, Delbruck noticed that in the prison, where the epidemic had developed very largely, the wells communicated with the drains. At Brachsted the epidemic arrested itself just as soon as a suspected well was closed. Delbruck explained the less intensity of the epidemic of 1867, compared with that of 1866, by the fact that the carrying of the water had been modified. Water was furnished almost pure in 1867, while up to the autumn of 1866 the conduits carried the water from the Saale through a region where all the discharges of the city were scattered. Ballot also spoke of the influence of impure water on the spread of cholera in Holland. Snow, in England, and innumerable other writers in Europe, India, and America, lay the greatest possible stress upon impure water as the special means for the conveyance of the infective agent of cholera. (See the article on *Water*, in the present volume.)

The contamination of water played an extremely important part in the extension of cholera in Egypt in the epidemic of 1883. The Mussulman population of Egypt bathe very frequently, but they are not careful about the water that they use for drinking. At Damietta the water is exceedingly foul upon the points of the Nile from which the water-carriers fill their water-casks, and just at these places are the special spots selected for bathing. The houses along the bank discharge their foul material directly into the river, and drains carry to it discharges from other houses, and from the mosques. According to Koch, these mosques play an extremely important rôle in the spread of cholera. The German cholera commis-

sion was able at Damietta to examine a number of mosques, the description of the arrangement of which is as follows: Only that part of the mosque that is directed toward Mecca is used for prayers. At the other end is an open space, in the centre of which is a tank for bathing, and sometimes this water remains several weeks without being changed, and surrounding the basin are a series of urinals and closets. The discharges from the whole are passed into the Nile, so that it is not strange that the infected material should be transported by such a water supply.

In the "tank districts" of India the conditions appear particularly favorable for the propagation of cholera from the sick to the well. In these districts cholera is very prevalent. The region is low and the land upon which the dwellings are situated is made ground derived from the immediate neighborhood, leaving pools which constitute the "tanks." The drainage from the dwellings flows into these relatively or entirely stagnant bodies of water, which is also used for bathing and, in many cases, for drinking purposes.

The epidemic of 1884 furnished new proofs in favor of the spread of cholera through the agency of water. Messrs. Marey, Brouardel, and Thoinot especially insisted upon this point. Marey, at the sitting of the Academy of Medicine, October 14th, 1884, said: "Among the influences that can cause the spread of typhoid fever or cholera there is one that by its intensity dominates all the others—that is the contamination of public water supplies." If a number of epidemics of cholera be studied, it can be determined, in effect, that cholera easily follows watercourses; that it is especially along small watercourses that it is propagated, is most frequent and striking. In order to explain this, there are but two hypotheses that are possible.

First, brooks, torrents, or rivers flow in valleys that are often narrow and shut in, and the villages found there often can have no communication except with each other. When one is attacked, it is a perfectly simple matter that the others should be also in their turn. This explanation is very plausible; for certain cases, and some epidemics, can be explained in no other way. The great rivers, the large watercourses, along which are scattered regions attacked by cholera, serve for the propagation of this disease, like the great roads of travel, in this way only, that they are lines of communication frequented by travellers.

Second, water is certainly a propagating agent of cholera. It is the water of a torrent, a brook, or a small river, contaminated in one part of its course, that transports the disease to the inhabitants on its borders that drink of the water, and innumerable instances can be brought forward to illustrate this point also.

Proust (*loc. cit.*, p. 216) speaks of the choleraic agent having for its vehicle of transportation either the air or the water, but the evidence in favor of the air as one of the transporting agents of cholera is nothing, and the weight of scientific evidence of late years militates against such a means of transportation. Altitude seems to have but slight influence upon the development of the disease up to a certain point, although Farr (in the Registrar-General's Report on the Mortality of Cholera in England, London, 1852) has attempted to demonstrate that the mortality from cholera was in inverse proportion to the elevation. The objection to this is, that the less frequent occurrence of cholera on the most elevated points may be due to the fact that the less accessible points are more thinly inhabited.

Moisture, taken in connection with the subsoil water, is a favoring cause of the greatest importance, and observations in this direction have furnished the basis for Pettenkofer's theory of the connection of subsoil moisture with cholera.

The development of the epidemics of 1836 and of 1854 seemed to coincide with the period of greatest diminution of the subsoil moisture in Munich, and therefore the choleraic contagion with which the soil is impregnated appears to disengage itself more easily. Hirsch reached

a similar conclusion. Kreuzer, in 1855, at Vienna, and again Pettenkofer, at Munich, observed the same facts. Pettenkofer's theory differs from others, in that, putting aside the chemical composition of the earth, he attaches a special importance to its physical characteristics, its density, its porosity, etc. He considers that the condition of the subsoil of localities and of houses plays a rôle of special importance in the propagation of cholera, and upon this special cause he places the development of an epidemic, after an importation from without; and, studying almost exclusively the physical condition of the region, the compact or porous condition of the subsoil, he considers that not only the primitive earth, and the soils of the transition period, but also the secondary formations, produce immunity when they are exposed to air in the condition of rocks. On the other hand, every porous soil that is susceptible of imbibition can become easily impregnated with fluid, or with gas, and vegetable earths as well as silicious earths may form "fat," always moist, lands, throwing out continual moisture about them, favoring the diffusion of the germs of cholera. Where the soil is made up of a compact calcareous rock cholera never becomes epidemic, and a few cases observed in such situations as the result of importation, do not propagate the disease.

Pettenkofer's theory has two points that must be distinguished from each other.

First, the nature of the soil. The soil must be porous, easily permeable, and also easily impregnated by liquids and gas. This condition is a permanent one.

Second, the level of the subsoil moisture. This level being movable, the effect is variable; when subterranean waters have reached the maximum of their elevation, there is neither decomposition of organic materials nor throwing off of miasms. If the subsoil moisture descends to a lower level putrefaction begins, the miasmatic vapors are thrown off more intensely, and just at this time the epidemic reaches its greatest development. This second point of his theory, certainly an ingenious explanation of certain cases, appears to be much more hypothetical than the first, the question of the porosity of the earth.

To sum up, Pettenkofer's theory, while it scarcely has the value ascribed to it by him, certainly seems to afford a partial explanation of the propagation of cholera by means of the porosity and moisture of the earth.

Ninth, atmospheric conditions play a not very important rôle, although the influence of season is manifest, and, apparently, storms sometimes seem to aggravate considerably an epidemic.

Somatic Conditions.—Race or nationality has no influence upon the development of cholera. The special influences favoring it are those of misery, fatigue, cold, and depressing mental conditions, which, by diminishing the resisting power of the body, render it more susceptible to the influence of the epidemic. Collections of human beings, in other words, agglomeration, play a very considerable rôle in the propagation of epidemics; so also do methods of transportation. Railroads are often the means of propagation, as was the case in the instance of Altenburg, quoted above. The epidemic of 1865, in Paris, was started by a woman who left Marseilles, with a choleraic diarrhoea, and was attacked with cholera upon her arrival in Paris. Transportation by caravans does not give much chance for the spread of the disease, when the distance passed over is of great extent; in fact, a great desert is the best of all obstacles to the propagation of cholera. In ships are most often found united the conditions of crowding and confinement favorable for the development of the choleraic agent.

Proust appears to believe that these elements do not have much potency if the entire ship's company come from the same infected region—in other words, have acquired an immunity in a choleraic focus; but if the ship's company has received a partial renewal, if new persons have come on board among the acclimated passengers, cholera finds a new favorable medium for attack, and, if aiding circumstances appear, the ship may become the centre of an intense epidemic. He goes on to speak of

this "law of accustoming," in what takes place in armies, the great fairs, and the pilgrimages; for when cholera is carried into these great collections, if the mass of people have not undergone the "choleraic acclimating," the explosion of the disease is rapid and the mortality considerable, but only continues for a few days, and ceases soon. The Crimean War furnishes an example of the rapidity of development and intensity of the disease among vessels free from the choleraic influence.

At the commencement of April, 1855, there reached Constantinople from France, fifteen to twenty thousand troops, made up in part of the Imperial Guard. These troops had not, during their voyage, a single case of cholera among them. They camped on the heights of Masslak, in an extremely healthy situation, and at that time there were in the city of Constantinople but very few traces of cholera. The rolls of the French military hospitals gave only fifty-three cases during March, and the roll of April 11th showed none. In the Crimea the cases of cholera were also very few, and nevertheless the troops were hardly settled at Masslak when, on the night of April 14th and 15th, cholera broke out among them, and a severe epidemic followed.

Fauvel ("Memoire lu à l'Acad. des Sciences," Paris, 1883) sums up this question of immunity in the following propositions:

"1. The ports of India that are the seat of endemic cholera are never the scene of a great epidemic.

"2. This fact relates to the general, but not absolute, immunity enjoyed by the native population of these parts.

"3. This immunity does not exist in the endemic localities for strangers who are in a condition favorable for contracting the disease. These are especially the Mussulman pilgrims who come to Bombay to embark for Mecca.

"4. The epidemics of cholera that develop in India, in the regions where the disease is not endemic, come from the places where it is endemic, and are favorable for attacking the Hindoo pilgrimages.

"5. The epidemics observed among the pilgrims to Mecca can also be traced to the localities where cholera is endemic.

"6. A severe epidemic of cholera confers upon the country or upon the locality which it has attacked a more or less complete immunity, which is more or less durable, and of which it is impossible to formulate the law for Europe, but which in India appears to last for a number of years.

"7. In the Hedjaz, and in the sparsely populated parts of Arabia, cholera has but a feeble tendency to propagate itself among the native population.

"8. The fact of the existence of a great epidemic of cholera in any country whatever is a proof that cholera is not there endemic."

To sum up, new scientific facts bear upon the question of immunity and make them clear upon a side hitherto unknown. The etiology and prophylaxis, in especial, of cholera receive from these facts new indications, and these facts also appear to be the expression of a law that includes an entirely different category of infectious diseases, which leave after them an immunity of a greater or less extent.

Period of Incubation.—The question of the period of incubation of cholera gives rise to a great deal of discussion. It appears, however, that in the immense majority of cases a period of a few days is sufficient for the incubation, and that sometimes this may require only a few hours. This fact is easy to observe if the beginning of the disease in a city or upon a ship be studied.

The Cholera Conference at Constantinople concluded as follows: "That all the facts cited in regard to a period of incubation longer than a few days are based upon cases that are not conclusive, either because the premonitory diarrhoea was comprised in the period of incubation, or because the infection could have occurred after the departure from the infected locality." The following is an instance:

On November 3d, 1848, upon the ship *Swanton* there were two hundred and eighty-nine emigrants for New Orleans, and the cholera did not break out on board until November 25th—that is to say, the twenty-third day of the voyage—and occasioned thirteen deaths. A certain number of these emigrants came from points in Germany where the cholera existed. This long period of incubation can be explained upon two hypotheses: either the passengers had with them clothing soiled with choleraic materials, which, placed in a confined air, could transmit cholera; or certain of the individuals embarked might have been affected at the time of their embarkation with a diarrhoea that might later have developed into true cholera. The duration of this premonitory diarrhoea has been much discussed, and in general it has been concluded that it does not last more than three days, and when it does pass this period, it is rarely prolonged beyond a week, and that therefore an individual isolated from all sources of contamination, and in whom the diarrhoea should be prolonged more than eight days after this isolation without presenting any characteristics of cholera, could be considered non-choleraic. But Griesinger among others dissents from this opinion, and declares that the period of incubation of cholera may be much longer. A bacteriological examination furnishes the only method of settling the question.

The experience of those who carefully studied the epidemic in Hamburg in 1892-93 points to an incubation of not less than twenty-four hours. After this period there may be a diarrhoea which attracts little attention, but which is in reality the first stage of the disease. In other cases the onset of symptoms may be very sudden, leading to collapse and death within a few hours. It has been noted that in the early days of an epidemic the spirillum develops more slowly in artificial media than is the case later in the course of the epidemic.

DESCRIPTION OF THE DISEASE.—The clinical manifestations associated with the presence of the cholera vibrio in the intestinal contents are so various that it is impossible to give a single clinical picture of Asiatic cholera. During epidemics of the disease this micro-organism has frequently been isolated from the feces of people presenting no evidence of any disturbance in health. In other cases its presence is associated with symptoms of the most marked character, followed by a speedily fatal issue. These facts by no means throw doubt upon the etiological significance of the cholera vibrio; for similar observations are well known in other infectious diseases, such as diphtheria, typhoid fever, and even infections with pyogenic micro-organisms.

Cases in which the cholera vibrio is present in the digestive tract without being associated with symptoms are of great sanitary importance, because this very absence of all manifestations of disease renders the spread of the infection from place to place very difficult of control or detection. It is also important to the individual himself. There are cases on record in which people in apparently perfect health have left regions where cholera was epidemic, have remained for a time free of any signs of ill health, and then, as the result of some dietary indiscretion, have suddenly succumbed to an attack of severe cholera, with the vibrios in the alvine discharges. It appears evident that in such cases the cholera vibrios in the intestine are virulent, but that the resistance of the individual was so great as to prevent the usual effects of infection until some additional factor created a susceptibility. It is not possible to state the frequency of such latent infections in times of epidemic cholera, but where the spread of the disease takes place through a contaminated water supply it is reasonable to suppose that they must be more frequent than could be indicated by any statistics as yet in existence. Rumpf, in his studies of the epidemic in Hamburg in 1892-93, reports that cholera vibrios were found in the feces of 62 individuals during the small after-epidemic of 1893, and that of these 19 failed to show signs of any great constitutional disturbance. These cases were studied because they had been closely associated with cases of pronounced cholera in the

city or upon vessels in the port. On the other hand, between February 23d and June 1st, 1893, 70 cases of diarrhoea were investigated to learn of the presence of cholera vibrios in the discharges, with negative results.

Leaving out of further consideration these important latent infections, we may divide cases of cholera into three groups, according to the severity of the clinical manifestations: First, choleraic diarrhoea, in which the symptoms present little beyond a marked looseness of the bowels; second, cholera, characterized by vomiting and considerable constitutional disturbance as well as diarrhoea with rice-water discharges; and, third, algid or asphyctic cholera or cholera gravis, which has hitherto served as the type of the disease.

These terms are not used to denote nosological entities, but merely to furnish concise expressions for clinical differences dependent upon variations in the relations between the virulence of the infection and the susceptibility of the patient. In individual cases the less severe forms of the disease may pass into the graver types, where conditions arise which modify these relations. In many epidemics the milder types occur most frequently early in the history of the epidemic, to be succeeded by a larger percentage of severe cases at the height of the epidemic, which are in turn followed by a preponderance of the milder cases as the epidemic draws to a close. These clinical observations harmonize with the experience that cultures in artificial media grow less rapidly early and late in an epidemic than at its height.

Choleraic Diarrhoea.—In the milder cases the stools are feculent or bile-stained and watery, are unaccompanied by much pain, and differ considerably in frequency in different cases. The symptoms usually first appear at night and are accompanied by some flatulence. The general health may remain good. In severer cases the stools are more numerous; the appetite is lost; the tongue becomes coated, and there is a feeling of gastric depression. The amount of urine is decreased. The patient becomes restless and suffers from headache. Dragging pains in the calves may be troublesome. These symptoms last a few days, and in favorable cases then subside. The course of the affection depends largely upon collateral circumstances. Indiscretions in diet, over-fatigue or imprudence of any kind exert an unfavorable influence upon the patient, and in many cases this choleraic diarrhoea passes into the severer forms of cholera. Although the cholera vibrios are regularly found in the discharges, the latter do not acquire the rice-water character typical of the severer forms of the disease.

The affection may prove fatal in people of diminished resistance; in the young or aged death being the result of exhaustion; but recovery is the rule.

Cholera.—Sometimes this type of cholera is preceded by the form just described, but more often the first symptoms noted are general malaise, loss of appetite, and nausea. The stools then become more frequent. They are at first feculent, but soon become more liquid and then assume the "rice-water" character of those in severer cases of cholera. These discharges consist of a serous fluid, rendered turbid by large quantities of desquamated intestinal epithelia, and frequently tinged more or less pinkish by red blood corpuscles. When examined microscopically the spirilla may frequently be seen in great numbers, but in many cases they cannot be made out as such, but appear as granules of various shapes. In addition to the symptoms mentioned above, vomiting comes on early in this form of the disease. After the stomach is emptied of food, the vomitus is a thin fluid containing some bile, or it may be colorless. Pain in the epigastrium, headache, and thirst appear as the disease progresses. The quantity of urine is reduced and albuminuria appears. The skin is cool and the volume of the pulse diminished.

Cholera may pass into algid cholera, or the symptoms may gradually subside and recovery follow; but not infrequently convalescence is delayed by a long period of debility and mental hebetude, resembling the typhoid stage of algid cholera.

Cholera Gravis; Algid or Asphyctic Cholera.—In this form, which has usually been regarded as the typical manifestation of the disease, the attack may suddenly develop, its onset being marked by great uneasiness, repeated discharges from the bowels, followed by syncope. This attack may overtake the victim while walking on the street in apparently good health. It is often preceded by a state of vague suffering, rapid prostration, deep colicky pains, anorexia, sometimes a diarrhoea, profuse sweats, disturbance of the senses, and more or less retardation of the pulse. After the development of the disease the symptoms follow each other in such a way as to allow of a division into two distinct periods.

First Period.—This is marked by an increase in the number of dejections and acts of vomiting; a flux is established which is at first serous or slightly bilious, and afterward becomes "choleraic." This term is used to designate those characteristic discharges of cholera which are liquid, whitish, grumous, sometimes resembling unclarified whey, sometimes a decoction of rice or oatmeal, and sometimes thickened meal, and nearly clear, which emit an insipid spermatic odor, and sometimes present traces of blood or bile. These evacuations are rarely absent, often continuing to the termination of the disease. Burning thirst, pain in the epigastrium, and prolonged hiccough are usual accompaniments. Intense cramps of the limbs occur, particularly in the calves of the legs; the muscles are often in a state of tonic contraction. Spasmodic movements, as involuntary flexion and extension of the fingers and toes, may often be seen. The pulse is very feeble, often imperceptible. The features are altered, trembling and great agitation come on, the pulse becomes suppressed; bluish spots appear, first upon the extremities; the skin becomes blue or black almost everywhere; the nails are livid and almost black, the fingers wrinkled, and the genital organs retracted. The volume of the body diminishes rapidly and perceptibly; the eyes sink in and are dull, with a bluish circle surrounding them; the conjunctiva fades, respiration is slow and feeble, the breath cold, and the pulse is reduced to a mere oscillation. The secretions are arrested, especially the urine, the voice is reduced to a whisper, the nose is cold and—rarely—gangrenous, the cornea is flattened and puckered; spots of blood appear on the sclerotic, viscid sweat on the face and limbs; the intellect becomes obscured, respiration is embarrassed, hiccough commences, and death follows, in the midst of an apparent calm. This is called the *cold, livid, or asphyctic* period. When patients escape death in this stage they enter upon the

Second Period.—In this the coldness ceases to increase, warmth returns, the pulse improves and gradually becomes febrile, the face regains color, the eye becomes animated, and a general reaction occurs.

If recovery is to be easy and rapid, vomiting becomes less frequent, the diarrhoea remains, but the discharges no longer present the appearance peculiar to the disease; the secretion of urine returns, nausea, thirst, and pains in the stomach cease to be felt, the pulse becomes regular, and convalescence begins.

If reaction is incomplete, the cold stage returns with renewed severity, or, on the other hand, if reaction be too severe, such accidents may occur as apoplexies, spasms, convulsions, local congestions and inflammations, and occasionally latent pneumonia. Stupor is sometimes present, with some of the signs of the last stage of typhoid fever. Swelling of the parotid glands and various skin affections, as roseola, urticaria, erythema, erysipelas, etc., may appear toward the close of the disease. The average duration is from one to three days, but sometimes death occurs in less than six hours, and is occasionally delayed a long time—in one case for fifty days.

Complications and Secondary Affections.—Complications are rare, and apparently accidental, but secondary affections, either direct results of the cholera or due to increased susceptibility to infection or to debility, are common.

Course, Duration, and Termination.—If death does not

occur during the algid stage, a peculiar transformation in the disease takes place and *reaction* sets in. This reaction varies in different cases, being slow and tedious in some, and abrupt and rapid in others; its course is not essentially modified by any antecedent disease, even those occurring as complications.

In the vast majority of cases cholera runs its course with great rapidity, the greater number of attacks lasting from eighteen to twenty-four hours, the shortest from one to six hours, and the longest from fifteen to twenty days. Its duration is the shortest at the height of an epidemic.

The termination of epidemic cholera may be favorable, the progress of recovery varying widely in different cases; it may be complete in a few hours even, and the patient may return to his ordinary occupation; on the other hand, it may be delayed until after a long and perilous struggle against complications and secondary affections. There may remain a general debility such as is not often seen after any other disease; the emaciated features, languishing expression, capricious appetite, obstinate gastralgia, colic, wakefulness, tendency to coldness, partial or general, and intellectual and moral dejection persist for a long time. An attack has been known to change the whole constitution and temperament of a patient. One attack appears to furnish no immunity against another, and relapses are always to be feared.

SYMPTOMS IN DETAIL.—Besides this general account of the disease the symptoms should be briefly discussed in the order of their occurrence.

Precursory Phenomena.—An attack is often preceded by initiatory uneasiness, which should attract attention; such are languor, pallor, anxious expression, sunken features, weight in the stomach, and movements of the intestines. Then vertigo follows, with abdominal pain, dimness of vision, and difficulty of hearing; the eyes become more brilliant than ordinary, like those of a drunken man. Sometimes circulatory disturbances are the first phenomena of the disease, marked by bluish circles around the eyes. In other cases, the progress of the preliminary symptoms differs—there are diminution of appetite for several days, general disagreeable sensations, and frequent alvine dejections, without pain, which are yellowish, more and more fluid, and, finally, become almost like water. A diarrhoea like this may occur without any other symptoms and develop into a severe case of cholera. Lastly, the disease may come on suddenly, and without warning overwhelm the victim with its full force—this often occurring at night.

Diarrhoea.—This is most frequently the mark of the onset of the disease, and when it is so, the stools become at once more and more frequent. Fifteen, twenty, or more dejections in twenty-four hours are usual, and in some cases (these are fatal) the evacuations occur in an almost continuous and involuntary jet. They are often accompanied by colic, borborygmi, and gurgling, either spontaneous or excited by pressure upon the abdomen. They are at first made up of bilious, fecal, or sero-mucous matter, but soon assume the characteristic appearance, viz., that of a whitish flocculent fluid such as has already been described. A large flocculent sediment is deposited from this fluid, a part of it looking remarkably like cooked rice. The fluid is blood-serum, and the sediment is made up of the epithelial lining of the intestines and of mucus. Sometimes the evacuations are tinged with blood-coloring matter, giving them the appearance of the lees of wine, or they may be of a deep brownish color from the same cause. The frequency of the dejections is not always increased with the progress of the disease, they are occasionally completely arrested during the cold period, and death may occur without their beginning again; on the other hand, they may return with increased violence. In those cases in which the acute attack is followed by a prolonged period of depression, during which the patient presents the typhoid state, the choleraic discharges give place to loose, diarrhoeal evacuations having a fecal odor. These may be frequent and persist for a number of days, gradually diminishing as convalescence advances;

but the typhoid condition is always favorable to the development of dangerous complications, and cases of cholera which take this form are by no means favorable. The abundance of the renal secretion is considered a valuable prognostic sign. After recovery obstinate constipation may occur.

Vomiting.—Nausea and vomiting, sometimes almost constant, occur from the very beginning of the disease. The vomitus is poured out by an almost constant effort; it does not differ in character from the dejecta, except that it is sometimes more limpid, and is sometimes slightly tinged with bile. It is very rare that vomiting persists to the second period of the disease, but the ingestion of the smallest quantity of fluid may excite it with great violence. It often alternates or coincides with a very troublesome hiccup.

Abdominal Pain.—This often precedes the vomiting and choleraic diarrhoea. It is gripping, and of the most intense character, situated in the region of the epigastrium, or over the entire abdomen. A doughy sensation is communicated to the hand upon pressure, and percussion gives, usually, an almost universal dull or flat note.

Anorexia; Thirst; Tongue.—Loss of appetite is complete, and corresponds in point of time with a burning and inextinguishable thirst. The throat and mouth are parched, the tongue is frequently clean, commonly large, pale, moist, cold, very rarely dry, and occasionally covered with a yellowish coat. This condition is peculiar to the first period; it varies, later on, with the degree of reaction, or with the nature of the complications and secondary affections.

Urine.—Upon the first appearance of the gastro-intestinal evacuations the urine becomes scanty, and is frequently completely suppressed; exceptional cases are reported in which it remains normal throughout. Emission is involuntary. Sometimes, after suppression, it reappears about the middle of the cold stage; being again suppressed for the remainder of the disease. The desire to urinate remains, although the power may be lost; the secretion and flow are generally re-established during the period of reaction. There are no observations pointing to the occurrence of renal disease. The urine is especially rich in indican and other ethereal sulphates. Ammonium salts are also increased and aceto-acetic acid may be present in considerable quantities. These changes in the urine are attributable to the ready absorption of putrefactive products from the intestinal contents, due in part at least to the loss of the epithelial lining of the bowel, and to the reduction of oxidative processes within the body.

Cramps.—Violent and prolonged cramps, beginning with the first diarrhoea, in the muscles of the legs and extending to the abdomen, arms, and even to the face, are among the most characteristic, and at the same time the most terrible, symptoms of cholera. They sometimes persist throughout an attack, and even after a cure, and muscular contractions have even been observed after life was extinct. During an epidemic cramps have been observed without any other symptoms. It has been suggested (Weir Mitchell: "Injuries of Nerves," p. 52, ed. 1872) that they are caused by the loss of water from the body, and the consequent "drying" and irritability of the nervous system, a phenomenon analogous to the violent contractions of a frog's leg when the sciatic nerve is exposed and allowed to dry in the air.

Headache; Derangement of the Senses.—Weight in the head, with giddiness and vertigo, occurs during the invasion; cephalalgia, often very severe, appears during reaction; it is generally heavy, and more marked in the frontal regions; at the same time occur ringing and buzzing in the ears. The sight is generally affected during the whole course of the disease; it is blurred, double, or perverted, so that the patient sees objects colored blue, or alternately black and red; it is occasionally completely extinct. The touch and general sensibility are much blunted.

Intellectual Faculties.—These are generally unaltered, although the power of expression may be impaired. It

is only in certain modes of reaction in the second stage, and in certain complications, that stupor and, more rarely, delirium occur.

Strength.—There is in all cases almost entire loss of strength, the least displacement of the limbs being unbearable. Most patients, either stretched on the back or with the limbs closely drawn up, remain in a state of complete immobility through fear of fatigue. Transient faintness appears in some cases.

Voice.—It is characteristic; changing very rapidly from a state of feebleness at the commencement of the disease to a rough and whistling tone. It occasionally becomes entirely extinct, but in some cases retains strength enough for loud cries. It gradually returns to its normal condition as the disease lessens in intensity and recovery progresses.

Respiration is ordinarily very difficult, the frequency varying from ten to fifty-two per minute. This does not depend upon any altered condition of the lungs as revealed by physical examination, but seems to be in some way connected with the presence of less than the normal amount of carbonic acid in the expired air.

Circulation.—The circulation is very gravely affected. The pulse becomes more and more feeble, and disappears entirely at the height of the cold period; it is always more frequent than in health. The blood moves slowly and will not flow from a vein or an artery of small size. This sort of stagnation aids in producing the bluish hue peculiar to the cold stage. This bluish hue makes its appearance first in the extremities, in the genital organs, and in the face. It is especially observable in patients who are plethoric and of florid complexion. It diminishes and often disappears during reaction, and sometimes does not occur at all. It may go so far as to produce gangrene, as has been observed in the nose, tongue, and sexual organs.

Temperature.—The temperature is seemingly reduced; the expired air being only 25° to 27° C. (77° to 80.6° F.). This reduction in temperature is confined to the surface, however, the internal temperature being higher than in the highest fever (Guterbock, *Virch. Arch.*, xxxviii, p. 30).

Appearance.—The aspect is characteristic; the face is contracted, the brow wrinkled, the cheeks are hollow, the lips thin and pressed in upon the teeth, the complexion becomes livid and bluish, the eyes more and more sunken, and surrounded by a dark circle. Expression is lost by degrees, and death seems to have occurred while life is still present. The eye is dim, its surface wrinkled, sunken, and sometimes dry, the globe is left exposed by the lids, and the conjunctiva becomes injected and covered with spots of blood. Even if recovery takes place, the normal aspect of the face returns very slowly.

COMPLICATIONS, SECONDARY AFFECTIONS.—*Complications* are rare and apparently accidental; among them peritonitis, jaundice, gangrene, œdema of the lungs, erysipelas of the face, abscesses, ulceration of the eyelids, and aphthæ may be mentioned as of occasional occurrence.

Secondary affections are, however, very common. They may consist of gastro-intestinal inflammations, immediate, or after some days of convalescence, or of affections of the respiratory organs. In other cases persons who have apparently escaped the accidents of cholera have a secondary fever, described as of a typhoidal type, dry skin, tension and tenderness in the epigastrium, jactitation, dry tongue, bilious stools, and chills. Various skin eruptions occur, and temporary albuminuria has been observed following an attack of cholera. The most grave of the secondary affections, however, are those which affect the nervous system. The cerebral congestions during reaction are, in some cases, followed by a typical meningitis with trismus. Rayer's "État cérébral cholérique" includes a group of phenomena distinct from those of meningitis, which supervenes upon the cold stage; the skin is cold, the pulse feeble, the head heavy, the countenance stupid, and sometimes the cholera tint remains. Other affections are

a sort of non-febrile delirium, lasting for two or three days, and the spasmodic contractions of the forearm which occur during convalescence. True intermittent febrile attacks, with initial chills, occurring every day during reaction, have also been observed. All these affections are, for the most part, more rapid than when occurring in the individual previously healthy.

PATHOLOGY.—Until more is known of the exact nature of the toxic substances which can be elaborated by the cholera spirillum, when present in the human intestine, no very exact statements of the pathology of the disease can be given. It is evident that an irritation of the intestinal mucosa, with more or less damage to the histological structures, is caused by the spirillum or its products, and that in pronounced cases a very abundant transudate of fluid follows. Many of the symptoms of the disease, especially in the algid stage, are due to the consequent loss of fluid on the part of the blood and tissues of the body. In addition to this loss of fluid there are reflex nervous influences upon the heart and perhaps other parts of the body, due to the lesions in the intestine, and toxic substances absorbed from the intestinal contents probably act upon the cells of the viscera. To these factors, *i. e.*, loss of fluid, nervous reflexes and toxæmia, which account for the symptoms of the disease, may be added an increased susceptibility to secondary infections.

PATHOLOGICAL ANATOMY.—The alterations of the internal organs in a case of death from cholera bear little relation to the violence of the disease. The appearances are about as follows: Emaciation is general, and there is marked lividity of the lips and nostrils. Rigor mortis is not rare before the warmth of the body has wholly departed and is very marked and prolonged. The peritoneal surface is sticky and covered with a viscid exudation (present in 91.6 per cent. of 530 cases); the vessels of the mesentery are engorged with blood. The calibre of the intestinal canal is more often increased than diminished, and always contains some fluid choleraic matter. The fluid is blood serum, containing a variable number of red corpuscles, and the thicker material found in it is made up of intestinal epithelial cells and mucus. The intestinal mucous membrane is usually normal in thickness, but is generally denuded of epithelium. The villi are swollen, giving the surface a velvety appearance, and Peyer's patches and the solitary follicles are much enlarged. The glands of the stomach and of the duodenum are enlarged, and the surface is largely denuded of epithelium. There are no special lesions of the other organs. The liver is rarely enlarged, is the seat of moderate cloudy swelling, and is usually congested with dark thick blood. The gall-bladder generally contains bile, which is at first thicker than normal, but subsequently becomes more abundant and pale. The biliary duct is not obstructed. The pancreas presents no marked alteration. The spleen in rapid cases is small, hard, and wrinkled upon its surface, of a deep red color on section, and sometimes dotted with ecchymoses; in slow cases it may be slightly enlarged and less deep red in color. The blood is thicker than normal, coagulates slowly, and the separation into clot and serum is very incomplete. The corpuscles are not altered in shape, but there is a remarkable diminution in the proportion of water and neutral salts, and a decrease in the amount of fibrin and albumin. The heart is usually soft and flabby, the muscle degenerated, with ecchymoses in the pericardium. The left side is apt to be empty and contracted, the right distended with dark, thick blood. The arteries are, in general, nearly empty, the veins distended with blood. The pleura are very frequently coated with a glutinous, stringy substance, and ecchymoses often appear in the subpleural cellular tissue. The lungs are usually healthy, but presenting engorgements at the posterior portions; or they may contain pneumonic areas or abscesses due to inhaled vomitus. The bronchi are much congested, and may contain a white, stringy mucus, analogous to that found lining the intestinal canal. The condition of the brain and spinal cord, together with their appendages, is merely that of congestion without special lesion, although it has been

declared that there is a sensible increase in their consistency. The ganglionic system presents no change worthy of notice. The muscles are often engorged with blood, and a very marked reddish-brown discoloration of the bones and of the teeth has been noticed in those dying of asphyxia. Renal congestion is the marked alteration in connection with the genito-urinary tract, and the straight tubules are often completely stripped of their epithelium. The epithelium of the convoluted tubules suffers marked parenchymatous degeneration, even in cases of short duration. In those dying in the cold stage the bladder is empty and firmly contracted. The uterus usually shows a hemorrhagic endometritis, and abortion is the rule in pregnant women.

DESCRIPTION OF THE SPIRILLUM OF CHOLERA.—Asiatic cholera is without doubt due to a special organism—the so-called "comma bacillus" of Koch—this name being a misnomer, for the bacterium is not a bacillus, but a spirillum.

The parasitic nature of the disease was suspected for a long time. A number of observers had noted the presence, in the cells, of bacteria answering the description of this special one, but it was not until the advance in methods of observation had progressed a long way that it was possible to isolate the organism, and study it under artificial conditions in such a manner as to obtain the evidence necessary to connect it with the process as a causal factor. It was in the year 1883 that Koch first discovered and described the spirillum of Asiatic cholera, which he first found during his investigation in Egypt during the epidemic there, and studied further during the following winter in India.

The organism occurs especially in the small intestine, is generally wholly confined to the contents of the intestine and the glandular cul-de-sac, but is occasionally found in the intestinal walls. It is exceptional to find it in any other part of the body, and it is not strange that investigations undertaken with the idea that cholera was a generalized disease were not productive of results. The bacterium is found in large quantities in the dejecta, and sometimes—in fact not infrequently—in almost a pure culture.

In the intestines and in the dejecta it presents the appearance of a short, thick rod, slightly curved in the long diameter, hardly half as long, but considerably thicker than the bacillus of tuberculosis. It usually occurs in this situation singly, but not infrequently it is arranged in pairs, with the curves opposed to each other, and thus recalling the shape of the letter "S." There are many exceptions to this rule, and a simple microscopical examination of the dejecta does not suffice to establish a diagnosis of Asiatic cholera, or to exclude such a diagnosis. Sometimes no curved, S-shaped, or spirillum organisms are seen, but the preparation contains numerous granules of various shapes. If, however, plate cultures are made from these discharges, they may yield practically pure cultures of the cholera spirillum. Even when very small quantities of the dejecta are used, the colonies may crowd the plates. Under cultivation in bouillon the organism appears longer and thinner, and there are many true spirilla to be seen in the preparations made from such a culture. (See Plate LIX.)

A characteristic that is of especial interest is its extreme motility, which has been demonstrated by Löffler to be due to a fine cilium or two, occasionally three cilia, which are longer than the bacteria, placed at one end of the organism. Shortly before division, both ends possess cilia. After prolonged artificial cultivation the motility is reduced in activity.

Shape and motility are not, however, sufficient to differentiate this bacterium from others with similar characteristics—and there are many that possess such—but the method of development upon the various culture media is entirely characteristic, and, as shown by Koch, is all that is necessary for separating this one in particular from the others that resemble it. It liquefies gelatin, but it does this slowly, and at the same time a certain part of this liquefied portion evaporates, and as a result