A TEXT-BOOK ON THE PRACTICE OF MEDICINE.

SECTION I.

SPECIFIC INFECTIOUS DISEASES.

I. TYPHOID FEVER.

Definition.—An infectious disease, characterized anatomically by hyperplasia and ulceration of the lymph-follicles of the intestines, swelling of the mesenteric glands and spleen, and parenchymatous changes in the other organs. The bacillus of Eberth is constantly present in the lesions. Clinically the disease is marked by fever, a rose-colored eruption, diarrhœa, abdominal tenderness, tympanites, and enlargement of the spleen; but these symptoms are extremely inconstant, and even the fever varies in its characters.

Historical Note.—The dates 1813 and 1850 include the modern discussion of the subject. Prior to the former year many observers had noted clinical differences in the continued fevers. Huxham in particular, in his remarkable essay, had recognized varieties. In 1813 Pierre Bretonneau, of Tours, distinguished "dothiénentérite" as a separate disease; and Petit and Serres described entero-mesenteric fever. Trousseau and Velpeau, students of Bretonneau, were, in 1820, instrumental in making his views known to Andral and others in Paris. In 1829 Louis' great work appeared, in which the name "typhoid" was given to the fever. At this period typhoid fever alone prevailed in Paris, and it was universally believed to be identical with the continued fever of Great Britain, where in reality typhoid and typhus coexisted, and the intestinal lesion was regarded as an accidental occurrence in the course of ordinary typhus. Louis' students returning to their homes in different countries had opportunities of studying the prevalent fevers in the thorough and systematic manner of their master. Among these were certain young American physicians, to one of whom, Gerhard, of Philadelphia, is due the great honor of having first clearly laid down the differences between the two diseases. His papers in the American Journal of the Medical Sciences are undoubtedly the first in any language which give a full and

satisfactory account of the clinical and anatomical distinctions we now recognize. No student should fail to read these articles, among the most classical in American medical literature.

Louis' influence was early felt in Boston, to which, in 1833, James Jackson, Jr., had returned from Paris. In this year he demonstrated, in his father's wards at the Massachusetts General Hospital, the identity of the typhus of this country with the typhoid of Louis. He had already, in 1830, noticed the intestinal lesions in the common fever of New England. Though cut off at the very outset of his career, we may reasonably attribute to his inspiration the two elaborate memoirs on typhoid fever which, in 1838 and 1839, were issued from the Massachusetts General Hospital, by James Jackson, Sr., and Enoch Hale. These, with Gerhard's articles, contributed to make typhoid fever, as distinguished from typhus, widely recognized in the profession here long before the distinctions were recognized generally in Europe. Thus, the diseases were described under different headings in the first edition of Bartlett's admirable work on Fevers published in 1842.

The recognition in Paris of a fever distinct from typhoid, without intestinal lesions, was due largely to the influence of the able papers of George C. Shattuck, of Boston, and Alfred Stillé, of Philadelphia, which were read before the Société médicale d'Observation in 1838. At Louis' request, Shattuck went to the London Fever Hospital to study the disease in England, where he saw the two distinct affections, and brought back a report which was very convincing to the members of the society.

Stillé had the advantage of going to Paris knowing thoroughly the clinical features of typhus fever, for he had been Gerhard's house-physician at the Philadelphia Hospital, where he had studied during the epidemic of 1836. At La Pitié, with Louis, he saw quite a different affection, while in London, Dublin, and Naples he recognized typhus as he had seen it in Philadelphia. The results of his observation were given in an exhaustive paper which presented in tabular form the contrasts and distinctions, clinical and anatomical, which we now recognize.

In Great Britain the non-identity of typhus and typhoid was clearly established at Glasgow, where from 1836 to 1838 A. P. Stewart studied the continued fevers, and in 1840 published the results of his observations. In the decade which followed many important works were issued and more correct views gradually prevailed; but it was not until the publication of Jenner's observations between 1849 and 1851 that the question was finally settled in England.

Etiology.—Typhoid fever prevails especially in temperate climates, in which it constitutes the most common continued fever. Widely distributed throughout all parts of the United States and Canada, it probably presents everywhere the same essential character.

It prevails most in the autumn months. Of 1,889 cases admitted to the Montreal General Hospital in twenty years, more than fifty per cent

were in the months of August, September, and October. Of 1,381 cases treated during twelve years at the Toronto General Hospital, 761 occurred in these months (Graham). It has been well called the autumnal fever.

It has been observed to prevail most in hot and dry seasons. According to Pettenkofer, epidemics are most common when the ground-water is low, under which circumstances the springs and water-sources drain more thoroughly contaminated foci and are more likely to be highly charged with poison. It may be also, as Baumgarten suggests, that in dry seasons the poison is more disseminated by the dust.

Males and females are about equally liable to the disease, but males with typhoid are much more frequently admitted into hospitals.

Typhoid fever is a disease of youth and early adult life. The greatest susceptibility is between the ages of fifteen and twenty-five. Of 660 of the Montreal cases there were under fifteen years of age, 51; between fifteen and twenty-five years, 308; between twenty-five and thirty-five years, 153; between thirty-five and forty-five years, 43; between forty-five and fifty-five years, 6; and over fifty-five years, 9. Cases are rare over sixty. It is not very infrequent in childhood, but infants are rarely attacked. Murchison has seen a case at the sixth month. It is stated that the disease may be congenital in cases in which the mother has had the disease late in pregnancy.

As in other fevers, not all exposed to the infection take the disease, and there are grades of susceptibility. Some families seem more disposed to infection than others.

The Specific Germ.—The researches of Eberth, Koch, Gaffky, and others have shown that there is a special micro-organism *constantly* associated with typhoid fever. It is a rather short, thick, motile bacillus, with rounded ends, in one of which, sometimes in both (particularly in cultures), there can be seen a glistening round body, believed to be a spore; but these polar structures are probably only areas of dense protoplasm. It grows readily on various nutritive media, and on potato in a characteristic manner, as the growth is invisible. This feature is not peculiar however to the typhoid bacillus. It is difficult to differentiate from the *bacterium coli commune*, except by certain chemical tests. This organism fulfils two of the requirements of Koch's law—it is constantly present, and it grows outside the body in a specific manner. The third requirement, the production of the disease experimentally by the cultures, has not yet been met. Probably the animals used for experimentation are not susceptible to typhoid fever. The bacilli inoculated in large quantities into the blood of rabbits are pathogenic, and in some instances ulcerative and necrotic lesions in the intestine may be produced. But similar intestinal lesions may be caused by other bacteria, including the *bacterium coli commune*.

The bacilli produce various poisons, of which Brieger has described a ptomaine—typhotoxin, and Brieger and Fränkel a toxalbumin; but our

information on these substances is still very defective. Cultures are killed at a temperature of 60° C. It is not probable that the typhoid bacillus produces spores, but it resists drying for days. Bouillon cultures are destroyed by carbolic acid, 1 to 200, and by corrosive sublimate, 1 to 2,500.

In recent cases of typhoid fever the bacillus is found in the lymphoid tissues of the intestines, in the mesenteric glands, in the spleen, and in the liver. It occurs also in irregular clumps in the contents of the intestines and in the stools. The bacillus is said to have been found rarely in the blood, in the rose-colored spots (?), and in the urine.

Outside the body the bacilli retain their vitality for weeks in water. Whether an increase can occur is not yet finally settled. Bolton denies it, but the general opinion seems to be that such increase may take place to some extent. They disappear from ordinary water in competition with saprophytes in a few days. In milk they undergo rapid development without changing the appearance of the milk. They may increase in the soil and retain their vitality for months. They are not killed by freezing, but, as Prudden has shown, may live in ice for months. In many epidemics the bacilli have been detected in the infected water. The detection however of the typhoid bacillus in drinking-water is by no means easy, and the question in individual cases must be settled by experts who have had special experience with this germ. Both Prudden and Ernst have found it in water-filters.

Modes of Conveyance.—(*a*) *Contagion.*—Typhoid fever is certainly not a very contagious disease, but the possibility of direct transmission must be acknowledged. The poison is not given off from the skin or in the breath, but in the fæces. Practically only those persons are liable to contract the disease in this way who have to do with the stools or with the body-linen of patients. I have known several instances in which nurses appear to have been infected under these conditions.

(*b*) *Infection of water* is unquestionably the most common mode of conveyance. Many epidemics have been shown to originate in the contamination of a well or a spring. A very striking one occurred at Plymouth, Pa., in 1885, which was investigated by Shakespeare. The town, with a population of eight thousand, was in part supplied with drinking-water from a reservoir fed by a mountain-stream. During January, February, and March, in a cottage by the side of and at a distance of from sixty to eighty feet from this stream, a man was ill with typhoid fever. The attendants were in the habit at night of throwing out the evacuations on the ground toward the stream. During these months the ground was frozen and covered with snow. In the latter part of March and early in April there was considerable rainfall and a thaw, in which a large part of the three months' accumulation of discharges was washed into the brook, not sixty feet distant. At the very time of this thaw the patient had numerous and copious discharges. About the 10th of April cases of typhoid fever broke out in the town, appearing for a time at the rate of fifty a day. In all about twelve hundred people were affected. An immense majority of all the cases were in the part of the town which received water from the infected reservoir.

Milk also may be the source of infection. One of the most thoroughly studied epidemics due to this cause was that investigated by Ballard in Islington. The milk may be contaminated by infected water used in cleansing the cans. In fresh milk it has been shown that the germs grow rapidly.

Filth, bad sewers, or cesspools can not in themselves cause typhoid fever, but they furnish the conditions suitable for the preservation of the bacillus and possibly for its propagation.

(*c*) *Contamination of the Soil.*—Pettenkofer holds that the poison is not eliminated in a condition capable of communicating the disease directly, but that it must first undergo changes in the soil, which changes are favored by the ground-water.

It does not seem probable that typhoid fever is communicated by the air alone, as by the medium of sewer-gas.

Once in the intestinal canal the typhoid germs probably do not like the cholera bacilli increase in the secretions, but penetrate the epithelial lining and reach the lymphoid tissue, upon which they exert their specific action, causing a cell proliferation greatly in excess of the physiological process. The necrosis may be regarded as the result of the maximum intensity of the action of the bacilli—an action not confined to the lymphatic apparatus of the intestinal wall, but also met with in a typical manner in the enlarged mesenteric glands and in the liver and spleen.

It has not yet been definitely determined whether the constitutional disturbances in typhoid fever depend upon the toxalbumins produced in the growth of the bacilli, though this is in the highest degree probable.

Morbid Anatomy.—The statistical details under this heading are based upon sixty-four autopsies, a majority of which were performed at the Montreal General Hospital, and upon the records of two thousand post-mortems at the Munich Pathological Institute.*

Intestines.—A catarrhal condition exists throughout the small and large bowel, and to this is due, in all probability, the diarrhœa with the thin pea-soup-like stools. Associated with this catarrh there is during life some epithelial desquamation.

Specific changes occur in the lymphoid elements of the bowel, chiefly at the lower end of the ileum. The alterations which occur are most conveniently described in four stages:

1. *Hyperplasia*, which involves the glands of Peyer in the jejunum and ileum, and to a variable extent those in the large intestine. The follicles are swollen, grayish-white in color, and the patches may project to a distance of from three to five mm. In exceptional cases they may be still more

* Münchener medicinische Wochenschrift, Nos. 3 and 4, 1891.

prominent. The solitary glands, which range in size from a pin's head to a large pea, are usually deeply imbedded in the submucosa, but project to a variable extent. Occasionally they are very prominent and may be almost pedunculated. Microscopical examination shows at the outset a condition of hyperæmia of the follicles. Later there is a great increase and accumulation of cells of the lymph-tissue which may even infiltrate the adjacent mucosa and the muscularis; and the blood-vessels are more or less compressed, which gives the whitish anæmic appearance to the follicles. The cells have all the characters of ordinary lymph-corpuscles. Some of them however are larger, epithelioid, and contain several nuclei. Occasionally cells containing red blood-corpuscles are seen. This so-called medullary infiltration, which is always more intense toward the lower end of the ileum, reaches its height from the eighth to the tenth day and then undergoes one of two changes, *resolution* or *necrosis*. Death very rarely takes place at this stage. I have seen but one instance in my series—a girl, aged twenty-four, who died at the end of the first week with severe nervous symptoms and in whose ileum the lymph-follicles were greatly swollen, pitted and cribriform, but without necrosis. Resolution is accomplished by a fatty and granular change in the cells, which are destroyed and absorbed. A curious condition of the patches is produced at this stage, in which they have a reticulated appearance, the *plaques à surface réticulée*. The swollen follicles in the patch undergo resolution and shrink more rapidly than the surrounding framework, or what is more probable the follicles alone owing to the intense hyperplasia become necrotic and disintegrate leaving the little pits. In this process superficial hæmorrhages may result and small ulcers may originate by the fusion of these superficial losses of substance.

There is nothing distinctive in the hyperplasia of the lymph-follicles in typhoid fever. Apart from this disease we rarely see in adults a marked affection of these glands with fever. In children however it is not uncommon when death has occurred from intestinal affections. It is also met with in measles, diphtheria, and scarlet fever.

2. *Necrosis and Sloughing.*—When the hyperplasia of the lymph-follicles reaches a certain grade resolution is no longer possible. The blood-vessels become choked, there is a condition of anæmic necrosis, and sloughs form which must be separated and thrown off. The necrosis is probably due in great part to the direct action of the bacilli. The process may be superficial, affecting only the upper part of the mucous coat, or it may extend to and involve the submucosa. It is always more intense toward the ileo-cæcal valve, and in very severe cases the greater part of the mucosa of the last foot of the ileum may be converted into a brownish-black eschar. The necrosis in the solitary glands forms a yellowish cap which often involves only the most prominent point of a follicle. The extent to which the necrosis reaches is very variable. It may pass deep into the muscular coat reaching to or even perforating the peritonæum.

3. *Ulceration.*—The separation of the necrotic tissue—the sloughing—is gradually effected from the edges inward, and results in the formation of an ulcer, the size and extent of which are directly proportionate to the amount of necrosis. If this be superficial, the entire thickness of the mucosa may not be involved and the loss of substance may be small and shallow. More commonly the slough in separating exposes the submucosa and muscularis, particularly the latter, which forms the floor of a majority of all typhoid ulcers. It is not common for an entire Peyer's patch to slough away, and a perfectly ovoid ulcer opposite to the mesentery is rarely seen. Irregularly oval and rounded forms are most common. A large patch may present three or four ulcers divided by septa of mucous membrane. The terminal six or eight inches of the mucous membrane of the ileum may form a large ulcer, in which are here and there islands of mucosa. The edges of the ulcer are usually swollen, soft, sometimes congested, and often undermined. At a late period the ulcers near the valve may have very irregular sinuous borders. The base of a typhoid ulcer is smooth and clean, usually formed of the submucosa or of the muscularis.

There may be large ulcers near the valve and swollen hyperæmic patches of Peyer in the upper part of the ileum.

4. *Healing.*—This begins with the development of a thin granulation tissue which covers the base and gives to it a soft, shining appearance. The mucosa gradually extends from the edge, and a new growth of epithelium is formed. The glandular elements are reformed; the healed ulcer is somewhat depressed and is usually pigmented. Occasionally an appearance is seen as if an ulcer had healed in one place and was extending in another. In death during relapse healing ulcers may be seen in some patches with fresh ulcers in others.

We may say, indeed, that healing begins with the separation of the sloughs, as, when resolution is impossible, the removal of the necrosed part is the first step in the process of repair. Practically, in fatal cases, we seldom meet with evidences of cicatrization, as the majority of deaths occur before this stage is reached.

Large Intestine.—The cæcum and colon are affected in about one third of the cases (in nineteen of the sixty-four). Sometimes the solitary glands are greatly enlarged. The ulcers are usually larger in the cæcum than in the colon. Perforation of the cæcum is rare. The appendix may be involved. In my cases there was ulceration in two and perforation in one case. I dissected a case in Montreal in which the patient died three months after an attack of typhoid fever, and a localized abscess was found, due to perforation of the appendix. Death resulted from pylephlebitis.

Perforation of the Bowel.—In one hundred and fourteen cases of the two thousand Munich autopsies (5·7 per cent) and in fourteen instances in my series, the intestine was perforated and death caused by peritonitis. The perforation may occur in ulcers from which the sloughs have already

separated, or it may be directly due to the extension of a necrosis through all the coats. In only a few cases is the perforation at the bottom of a clean thin-walled ulcer. In one instance the perforation occurred two weeks after the temperature had become normal. The sloughs were, as a rule, adherent about the site of perforation. A majority of the cases were in small deep ulcers. There may be two or even three perforations. The orifice is usually within the last foot of the ileum. In only one of my cases was it distant eighteen inches. Peritonitis was present in every instance.

Hæmorrhage from the bowels occurred in ninety-nine of the Munich cases, and in nine of my series. The bleeding seems to result directly from the separation of the sloughs. I was not able in any instance to find the bleeding vessel. In one case only a single patch had sloughed, and a firm clot was adherent to it. The bleeding may also come from the soft swollen edges of the patch.

The *mesenteric glands* at first show intense hyperæmia and subsequently become greatly swollen. Spots of necrosis are common. In several of my cases suppuration had occurred. The bunch of glands in the mesentery, at the lower end of the ileum, is especially involved. The retroperitoneal glands are also swollen.

The *spleen* is invariably enlarged in the early stages of the disease. In only one of my cases did it exceed (600 grammes) 20 ounces in weight. The tissue is soft, even diffluent. Infarction is not infrequent. Rupture may occur spontaneously or as a result of injury. In the Munich autopsies there were five instances of rupture of the spleen, one of which resulted from a gangrenous abscess.

The *liver* shows signs of parenchymatous degeneration. Early in the disease it is hyperæmic, and in a majority of instances it is swollen, somewhat pale, on section turbid, and microscopically the cells are very granular and loaded with fat. Necrotic areas occur in many cases, as described by Handford. They have been studied recently by Reed in Welch's laboratory. No definite association could be determined between the groups of bacilli and the necrotic areas. In twelve of the Munich autopsies liver abscess was found, and in three, acute yellow atrophy. Diphtheritic inflammation of the gall-bladder is occasionally met with. This may lead to perforation and fatal peritonitis.

The *kidneys* show cloudy swelling, with granular degeneration of the cells of the convoluted tubules; less commonly an acute nephritis. A rare condition described by Rayer, Wagner, and others is the occurrence of numerous small areas infiltrated with round cells, which may have the appearance of lymphomata (Wagner), or may pass on to softening and suppuration, producing the so-called *miliary abscesses.* It is usually a late change. The bacilli have been found by some observers in these areas. The bacilli can be obtained by culture from the kidneys, and have been found in many instances in sections. They have also been found in

the urine in a few cases. Diphtheritic inflammation of the pelvis of the kidney may occur. It was present in three of my cases, in one of which the tips of the papulæ were also affected. Catarrh of the bladder is not uncommon. Diphtheritic inflammation of it may also occur. Orchitis is occasionally met with.

The anatomical changes in the *respiratory organs* are not very numerous. Ulceration of the larynx occurs in a certain number of cases; in the Munich series it was noted one hundred and seven times. It may come on at the same time as the ulceration in the ileum, but the bacilli have not yet, I believe, been found in the ulcers. They occur in the posterior wall, at the insertion of the cords, at the base of the epiglottis, and on the ary-epiglottidean folds. In the later periods catarrhal and diphtheritic ulcers may be present.

Œdema of the glottis was present in twenty of the Munich cases, in eight of which tracheotomy was performed. Diphtheritic laryngitis is not very uncommon. It occurred in a most extensive form in two of my cases. In one the membrane was chiefly in the pharynx, and extended only upon the epiglottis; in the other there was a uniform membrane which extended into the trachea and in the tubes of the second dimension. In eight cases in my series there was lobar pneumonia. Hypostatic congestion and the condition of the lung spoken of as splenization are very common. Gangrene of the lung occurred in forty cases in the Munich series; abscess of the lung in fourteen; hæmorrhagic infarction in one hundred and twenty-nine. Pleurisy is not a very common event. Fibrinous pleurisy occurred in about six per cent of the Munich cases, and empyema in nearly two per cent.

Changes in the Circulatory System.—Endocarditis is rare. It was not present in any of my cases, and existed in eleven only of the Munich autopsies, in which also there were fourteen cases of pericarditis. Myocarditis is not very infrequent. Dewevre,* in a series of forty-eight cases, found in sixteen granular or fatty degeneration, and in three a proliferating endarteritis in the small vessels. It is remarkable that even in cases of death from heart-failure, with intense fever, the cell-fibres may present little or no observable change. The *arteries* are not infrequently involved in typhoid fever. Barié distinguishes an acute obliterating arteritis and a partial arteritis, and states that they both occur most commonly in the arteries of the lower extremities. They are responsible, no doubt, for certain of the cases of blocking of the arterial trunks. This arteritis may affect the smaller vessels, particularly those of the heart. In the veins, thrombi are not infrequently found, particularly in the femoral veins, and more rarely in the cerebral sinuses.

Nervous System.—There are very few coarse changes met with. Meningitis is extremely rare. It was not present in any one of my autop-

* Archives générales de Médecine, 1887, 2.