

ENTERIC FEVER—ITS INFECTION, PATHOLOGY, AND PRESENT TREATMENT.*

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The more important advances made in the different departments of medicine in modern times appear to have resulted more or less directly from various discoveries and developments in the science of bacteriology. In this way not only has the domain of practical medicine and surgery been widely extended, and new fields opened for advanced work, but in like manner great improvements in the management of disease have resulted from bringing into more intelligent and better use much of the means acquired in former times.

A brief mention of certain points in the etiology, pathology, and treatment of the common infectious disease, enteric (typhoid) fever, as they are now understood, may illustrate. The wide prevalence and great mortality shown in the history of this disease give much importance to any discovery which promises improvement either in its management or in the means of its prevention.

TYPHOID IN THE PAST.

The time in the history of medicine when the disease designated as typhoid fever was first known is not determined; an account of its existence in medieval times appears in medical history. It is known to have prevailed in all countries and climates. Nearly fifty years ago the late Professor George B. Wood of Philadelphia, who had given much attention to the study of the disease, and was regarded as first authority in everything pertaining to it, declared that "nothing precisely is known concerning the cause of enteric fever. The circumstances of its production are very diversified. It is certainly often generated in institutions where human beings are crowded together, with insufficient or unwholesome food, or a confined and vitiated air." This was something of an approach toward an account, at least of what may be in part the sources of the disease; but a nearer advance toward a knowledge of the specific cause was made in later years, when its infectious character came to be better understood; in the light of which knowledge not only could a more definite view of the source of the disease be had, but more effectual means could be provided against the infection.

Progress was slow in determining the causes of infectious diseases before the time of the great advances of late years in the department of bacteriology. This advance was the beginning of a new era in medicine, the great light of which is now unfolding, the practical advantages of which largely appear in the intelligent means now used in the prevention as well as in the management of disease. It is known that a very common source of the typhoid germ is found in water, used for domestic purposes, whose sources of supply have suffered from sewage pollution; that it may be taken from milk and other articles of food which have been infected, and which are capable of for a time supporting the living germ of infection; also from the persons and clothing of attendants who have been careless in their manner of dealing, especially with the excretions of typhoid patients. There are many ways in which the substance of human excrement containing the disease germ may find its way into the bodies of persons not immune, and cause the infection. The following reports may illustrate.

Milk as a Vehicle.—An epidemic of typhoid occurred

in a Connecticut town, in 1895, in which in less than two months there were 406 cases, concerning which the statistics were given as follows: Epistaxis occurred in 117 cases; the characteristic skin eruption in 360; hemorrhages from the bowels in 73, with 12 deaths; acute nephritis occurred in 9 cases, of which 4 were fatal. Perforations of the intestine occurred 7 times, with 6 deaths. Relapses occurred in 26 cases. There were 27 deaths in the 406 cases. Careful investigation concerning the origin of the disease in this epidemic traced it to a single dairy, where the pans in which the milk was first kept were washed with water from a shallow well, which was found to be contaminated by a leaking through the earth from several privy vaults in the vicinity¹.

Oysters Infected.—A number of students of a New England college were taken at one time with enteric fever, and four deaths occurred. A search for the cause led to the discovery that all who had suffered from the disease had eaten raw oysters at a banquet. At the same time it was found that students from another college had been served with oysters from the same source, and had alike suffered from the disease. Further investigation revealed the fact that, although these oysters had grown in the deep waters of Long Island Sound, they had been transplanted and "fattened" in the shallow water of a creek, at a point 300 feet below the outlet of a private sewer coming from a house where there had been two cases of typhoid fever². This example shows the tenacity of life possessed by the specific microbe, in that its vitality is not readily destroyed even by salt water.

Further evidence of the vitality and of what may be the habitat of the typhoid germ has recently appeared³. In a locality where several outbreaks of the disease had occurred, examinations and experiments with the soil were made by a physician, the results of which were given as follows: He inoculated soil with typhoid germs, and from time to time took samples for investigation. He found that the typhoid bacilli were able to grow in certain soils, and that they could, under certain conditions, survive from one summer to another; the rains of spring and autumn and the frosts and snow of winter did not kill them. The part of the soil exposed to the sun showed no typhoid bacilli; but by scraping down one-sixteenth inch from the surface, organisms were found to be present. Cultures of the bacilli planted at a depth of eighteen inches grew to the surface, and others inoculated on the surface extended to a depth of three inches. It is possible that this downward growth may have been assisted by mechanical means, as rains and artificial watering. No lateral spread could be ascertained. Vegetation was detrimental to the healthy growth of the organisms.

As bearing on the probability of the source of infection here described, the writer has in mind a visit to a hospital in a city of one of the northern states, which was crowded with typhoid patients, most of whom had been laborers on the city's public works, working in trenches for water-mains and sewers. It is believed that prevalence of the fever, which was great in the city at that time, was due in part, at least, to infected soil. The rocky promontory on which a large portion of the city is built is mostly covered by a clay soil; but the impervious rock with its cup-shaped depressions, beneath the superficial layer of earth, continually held quantities of surface water which caused saturation of the contained soil, in many instances to the surface. The opening of some of these cavities by trenches cut

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through earth and rock, afforded a certain amount of sanitary drainage, and thereby was a valuable improvement; but it endangered the lives of laborers engaged in the work.

The public water-supply of this city, at that time, had been from the great lake on the shore of which the town is built. This also received the city sewage, and was credited with the return of a percentage of the same to the city through its public water-works. Thus it was that the water had its first opportunities for the direct infection of its consumers, and, secondly, was able to plant its surplus product in germ-producing culture-pots in the soil.

CONCERNING NOMENCLATURE.

An idea of what has been the history of the progress of medical knowledge of this disease may be had from what has appeared in the names which it has received. It may be said, in a general way, that in many instances the names which have been given to diseases, show not only the extent to which the nature of the particular disease was understood, and a proper estimate and classification made, but indicate something of the general status of medical science at the time of their origin.

Gaspard Laurent Bayle (1778-1816) of Paris, because of his important investigation, was called the "god-father" of typhoid fever; and Chomel (1788-1858), another French professor, devoted his time to the study of the disease to such an extent as to be designated the "Chomel of Typhoid Fever," but the term "typhoid"—like typhus—was made known by the French physician, Louis, whose work on "Typhoid, Putrid and Adynamic Fever" appeared in Paris about the year 1830. The term typhus, meaning stupor, was given to the fever which became known by that name, because of its apparent phenomena, showing a low or adynamic form of disease. M. Petit, also of Paris, had proposed the name, "entero-mesenteric fever," which looked more directly to a pathology and the location of the organic lesion which usually belongs to the disease. After Petit and Louis came Bretonneau, another Frenchman, who gave the name, "dothineritis," meaning pustule of the intestine. At the same time "follicular enteritis" came into use. Both of these terms had relation to the characteristic lesion usually found in the mucous membrane of the small intestine. It has been called "nervous fever," "continued fever," and "winter fever," for the reasons: 1, that the effects of the disease are manifest in the disturbance of certain functions of different parts of the nervous system; 2, that the want of distinct intermissions in the course of the disease precludes the idea of malarial poisoning as a cause; and, 3, because of its prevalence in the colder as well as in the warmer climates. The simple term "enteric fever," which is the name now generally preferred, was principally advocated by the late Professor Wood of Philadelphia, whose explanation concerning his choice of name was as follows: "It is merely intended," he said, "to express the fact that this fever is distinguished from all other idiopathic fevers by the frequency and extent of the intestinal disease. Other fevers are attended occasionally with the disease of the bowels; this almost always, if not essentially."

SYMPTOMS AND COURSE.

Only a brief outline of what appears as the characteristic phenomena of this disease is here necessary. As before intimated, it occurs in all countries and climates. Adults are more liable to the disease than young children, although the latter are not exempt. Its invasion is

generally insidious, and its development gradual. Languor, headache, increased temperature and accelerated circulation are usually present. In the early stage an alternation of temperature may occur with some regularity each day. The tongue may be coated at first, and, with the further advancement of the disease, may become dry and glazed, frequently with a brown stripe in the middle. In the further advancement, existing symptoms may become intensified and others may be added. The spleen almost invariably becomes perceptibly enlarged, the abdomen becomes distended and tympanitic, and small rose-colored spots appear on the surface. There is apt to be a certain degree of deafness, and an irritating bronchial cough is present; dark sordes form on the teeth, and a low form of delirium supervenes. Diarrhea is apt to occur, and hemorrhages from the bowels are not infrequent. These symptoms may be studied individually, in connection with the pathologic lesions found in the intestinal canal and in other of the digestive organs, and in the action of the disease on different parts of the nervous system.

PATHOLOGY.

We may best come to an understanding of the pathologic conditions found in the disease, by a brief notice of the history of former management and observation, viewed in the light of present knowledge. Although somewhat out of place here, an item of treatment may be mentioned for reasons which will appear.

A little more than seventy years ago Professor Wood advocated the use of the oil of turpentin in the treatment of enteric fever; this especially in cases in which the glazed and striped tongue, and tympanitic abdomen, perhaps with diarrhea and hemorrhage, indicated inflammation of the intestinal mucous membrane, with ulceration and danger of perforation of the intestinal glands⁴. Other means and medicinal remedies then used in treatment, some of which are still in use, were the following: evacuation of the bowels, to be secured at the onset if possible; the use of refrigerant and diaphoretic drinks, cold ablutions, small doses of mercury, counterirritation and poultices to the abdomen, and supporting measures, with stimulation when required. These remedial means and measures are here mentioned, not as giving a complete treatment for the disease, but rather as noticing the part of some of them in the therapeutics of the disease, based on its pathology as now understood.

Concerning the oil of turpentin, as a remedy, Professor Wood, in emphasizing his recommendation of its use, says: "I can not too strongly impress upon the profession my convictions of the importance of this medicine. It is to be employed in all cases of the disease when the tongue is dry. It acts in some measure as a stimulant, but chiefly, I believe, as an alterative to the ulcerated surfaces in the intestinal mucous membrane." Notwithstanding the fact that this recommendation of the use of this remedy was made by Dr. Wood many years ago, it is observed, nevertheless, that it has by no means been relegated to the past. It now appears as a most valuable germicide in the disease. No less authority than Simon of England, with others, is represented as "preferring this to other intestinal antiseptics that have been suggested". In the light of our present knowledge of the part of bacteria in the etiology and pathology of many diseases, and of the germicidal action of certain remedies, the term "alterative," formerly much used in therapeutics as a cover for what was not understood, has become quite obsolete. In explanation of the so-called alterative action of the oil of turpentin, and other remedies of this class, in conditions such as exist in the

intestinal canal and elsewhere in cases of enteric fever, we now have a knowledge of the specific action of these agents. In this way the oil of turpentin now comes to the front as a disinfectant and germicide remedy, whose properties render it especially useful, not alone in the destruction of the typhoid germ, but in aiding the repair of lesions on mucous surfaces, caused by the infection, as in the tissues of various organs. It is readily taken into the tissues, is found in the urine and other excretions, and is exhaled from the lungs.

Our present knowledge of specific pathogenic germs as disease-causes affords an understanding of much in pathology and therapeutics, which before could be known only in part—this from external appearances and apparent results. The advance of our knowledge of diseases, of which the one at hand is an example, has been from a theoretic basis for the pathology of disease, to the more satisfactory and substantial foundation in pathologic anatomy. We have in this case the specific germ known as the bacillus typhosus. It is in the province of bacteriology that most progress has been made in late years in the knowledge of the etiology and pathology of enteric fever. In the advance made by this means, however, enteric fever is but one disease among many.

AIDS IN DIAGNOSIS.

As important aids in the diagnosis, we now have what is known as the Widal-Johnson serum test, in which a drop of the patient's blood is made to show the characteristic reaction—this even when taken at the inception of the disease; and the Ehrlich's diazo reaction test, by chemical treatment of the urine. Of the latter it may be said that, while the specific reaction may be obtained in the urine of typhoid cases, it has also been found in the urine of persons suffering from other diseases, viz., pneumonia and pulmonary tuberculosis, acute articular rheumatism, certain forms of meningitis, and a few other acute inflammatory diseases. For this reason this test is valuable principally as an aid to be used in connection with other means of diagnosis. These tests are based on what appears in the bacteriology of the disease, and are found to be reliable when properly used.

NOTES ON PRESENT MANAGEMENT.

Prevention.—What is learned concerning the nature and physical properties of the agent of infection, in this as in other diseases, affords direction as to means of prevention. Immunity to the disease, either complete or partial, is natural in the bodies of certain individuals. The proportion of such to the number who are liable to the disease is unknown. Immunity acquired by artificial means is a quite possible thing in the future; it belongs to the great community depending for existence on what is called serumtherapy, is believed to have worthy parentage and respectable blood relations, but has not yet arrived at maturity; it is at best but an heir apparent.

Unlike any other infectious diseases, a common method of passing the contagion from one person to another in this is by allowing the lodgment of excrementitious matter, loaded with the infection, on persons, clothing, and articles of food, from and on which it finds its way to the alimentary canal. As preventive to this, chief importance is given to securing absolute cleanliness of patient and surroundings, and the careful disinfection and disposal of all excretions.

The advance of knowledge concerning the etiology and the means of prevention of this disease has correspondingly increased the responsibility of physicians and health authorities in the matter of its existence. A distinguished Chicago teacher gives expression to this

thought as follows: "With its mode of propagation now so well understood, continued prevalence of the disease is a reflection upon the civilization of the age in which we live;" and he declares that numbers of our profession are not doing all they are able to do in the direction of prevention. He emphasizes the importance of directing preventive means to the destruction of the immediate cause of the disease, and observes: "The usual media of infection are the intestinal discharges. These should be disinfected the moment they leave the body. . . . A 2 per cent. solution of carbolic acid, a 1-5000 solution of corrosive sublimate, or a 1-250 mixture of slacked lime, kills the bacilli of typhoid fever in fifteen to thirty minutes. The dejections of the patient should be received into a bed-pan containing such solution, and be thoroughly mixed with it, and allowed to stand an hour before being finally disposed of. The most watchful attention is to be given also to cleanliness of the patient's person." Further directions are given to the effect that after each evacuation, the parts liable to be soiled are to be bathed with a sublimate solution⁶.

Treatment.—Modifications which have properly been made in the treatment of enteric fever are based on the present known pathology of the disease—its part in bacteriology. In the light of present knowledge, it has been greatly simplified. It consists in well-managed drainage from the bowels; in the early stages of the fever suitable evacuates are in place, but caution should be observed in the use of cathartics in the latter progress of the disease. Principal importance is given to the use of such disinfectants as will best and most speedily rid the intestinal canal of the specific disease germ; including such therapeutic agent or agents as, like turpentin, will follow and destroy the microbe in the tissues of organs infected. The oil of turpentin is most acceptable in the form of an emulsion. Small doses of mercury are admissible, and are antiseptic. Carbonate of guaiacol has been mentioned as of first importance. The use of salol has been favorably noticed. Recently an English physician has shown good results from the use of compound tincture of benzoin. This accords with what has been made to appear by the use of other medicines of this class. Beechwood creosote is a good germicide in this affection, as well as in tuberculosis.

Concerning the effect of the cold bath in the treatment of typhoid fever, it is claimed by a French physician, Robin, that with the temperature lowered, a better oxidation takes place in the process of respiration, and that thereby the toxic products of tissue destruction are reduced to harmless, excrementary bodies.

In the matter of the Woodbridge method of treatment, so-called, the fact that in it antiseptic and eliminative means are employed is of more account than are the author's methods of presenting his claims to originality.

A general supporting and sometimes a stimulating treatment is necessary to counteract, if possible, the depressing effect of the toxins of the disease on the vitality of the nervous system. The fact that the disease primarily affects certain important functions of digestion and nutrition renders great care necessary in the dietary for different cases and stages.

Surgical Emergency.—Laparotomy, for the purpose of repairing the lesion of perforation of the intestine has been attended with a degree of success. Statistics of this complication and of the operation for the same were given by Armstrong, an Australian surgeon, in 1897, in substance as follows: Between 1 and 2 per cent. of all cases are given as having suffered from this complication, and above 6 per cent. of the mortality of the

disease has been due to this cause. In twenty-three laparotomies in cases of true typhoid, done for closing the perforation, recoveries were had in four cases. Notwithstanding this low percentage of recoveries, the operation has been advocated for the reason that without it there is a certainty of fatal result, but that some hopes are offered by this procedure. The advice is qualified by a proviso, that laparotomy should not be resorted to when the pulse is strong and not too frequent.

In view of the great mortality from perforation, notwithstanding what has been offered by surgical operation, advance is demanded in one of two directions, or in both, viz.: Either our understanding of the disease, its successful treatment, or means of prevention, must be so advanced and so widely and practically known as not often to allow the existence of the advanced stage of the disease in which this complication is liable to occur; or, if cases of perforation must sometimes necessarily come, the surgeon's early presence and the improved technic of his operative measures must be such as to materially reduce the rate of mortality of the past.

It is true of enteric fever, as of most other diseases, that the greater success in management depends largely on a knowledge of when, where, and how to act. The knowledge of conditions, means, and methods now available should guarantee results not reasonably expected in former times; and the assurance now is that the better time promised is already at hand.

BIBLIOGRAPHY.

1. Year-Book of Med. and Surg., 1897; Med. Rec., N. Y., Dec. 7, 1895.
2. Ibid., Dec. 15, 1894.
3. John Robinson: British Med. Jour., Jan. 8, 1898.
4. Wood, George B.: N. A. Med. and Surg. Jour., April, 1826.
5. British Med. Jour., March 21, 1896.
6. Wm. E. Quine: Medical Standard, March, 1899.

THE REVISION OF THE PHARMACOPEIA.*

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It is none too early for the medical profession to begin to discuss the revision of the "U. S. Pharmacopeia," which is to take place next year. While the actual appointment of delegates to the pharmacopeial convention rests with medical and pharmacal colleges, state societies and the three Government medical services, the revision should represent the opinion of the profession at large. This opinion can be expressed only by free discussion in print and in various medical meetings.

Within the last few decades a problem has arisen which successive pharmacopeial conventions have managed to ignore, but which must be faced in the near future. Up to 1860 or 1870, almost all drugs were either standard inorganic chemicals or vegetable substances which could be gathered by anyone with a working knowledge of botany, and which could be prepared for dispensing by very simple means. At present we are departing more and more from the older concept of galenicals, and are forced to adopt drugs requiring an elaborate knowledge of organic chemistry and special appliances for manufacture which can be economically employed only on a large scale. While the older animal drugs are few in number, and with one or two exceptions of little importance, animal extracts and antitoxins have recently increased the relative importance of the animal kingdom in pharmacy and a new departure must here be made by the future pharmacopeial revisers.

In regard to the use of galenicals, especially of the

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vegetable drugs, many physicians have passed through the following stages: 1. They have desired to know the effect and dose of any arbitrary preparation, for instance the tincture. 2. They have wished to have a standard preparation, such as fluid extract. 3. They have asked to know not how much of the crude drug was contained in a given amount of the extract, but how much of the active principle. 4. They have argued: "What is the use of employing the crude drug or a galenical at all? Give us the active principle and we will make our own dilutions." Twenty years ago, the triturate was introduced for the sake of having a 10 per cent. dilution of strong drugs. But, in practice, very few physicians have ever thought of the tablet as an official preparation, and they have ordered the amount of the active ingredient, without reference to whether the triturate contained ten times as much weight of sugar of milk or some other multiple. The abstract was dropped from the last edition of the pharmacopeia simply because those who were anxious for a standardized extract preferred the alkaloid itself, and those who did not were content with the old-fashioned extract of no particular strength. In fact, the day of galenical is waning, and we are aiming more and more at the isolation of active principles. There remain, however, several valuable drugs, like cannabis indica, digitalis and ergot, whose active principles have not yet been satisfactorily isolated for practical use. In such instances, and in many others for convenience or out of deference to the long-established habit, galenicals must be maintained.

Rather for the sake of eliciting discussion than to impress a personal opinion, I will briefly outline what seems to us an ideal treatment of galenicals by the Pharmacopeia. I do not intend, however, to convey the impression that I consider so radical a change from present standards feasible, immediately:

1. There should be one—and only one—active liquid and one solid preparation of each drug, adapted for internal use.

2. These preparations should be of definite strength, either with reference to the crude drug or the active principles. As the maintenance of galenicals is justified, rather because of the existence of drugs whose active principles can not be isolated, it would perhaps be wiser to standardize with reference to the assayed crude drug in all instances, as by adopting the fluid extract and abstract for all plants used internally.

3. All preparations for external use, including ointments, plasters, liniments and certain solutions, should be of safe, maximum strength for application.

4. For ointments, there should be duplicate or triplicate preparations, of the same active content but differing in base, so as to allow an organic fat and a mineral salve to be used at will, as well as, perhaps, an absorptive ointment containing wool-fat.

5. The physician should never be compelled to consult a pharmacopeial list to determine whether such and such a preparation of any particular drug be official. Every galenical should be official for every drug to which it is applicable.

6. Unless required by certain physical and chemical properties, there should be no galenicals or definite simple substances, whether inorganic or organic, with the possible exception of ointments. Whenever volatility or deliquescence or dangerous caustic properties require the use of a solution, it should be as concentrated as possible. This would apply to ammonia, hydrochloric acid, formalin, zinc chlorid, etc.

7. A wider range of vehicles should be adopted. Choc-