BREMER (L.)
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from John S. Billings.
with the writer's compts.

Typhoid Fever in the Light of Modern Research.

Facts and Doubts About Cholera.

BY
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ST. LOUIS, MO.

WITH TWO PHOTOTYPES.

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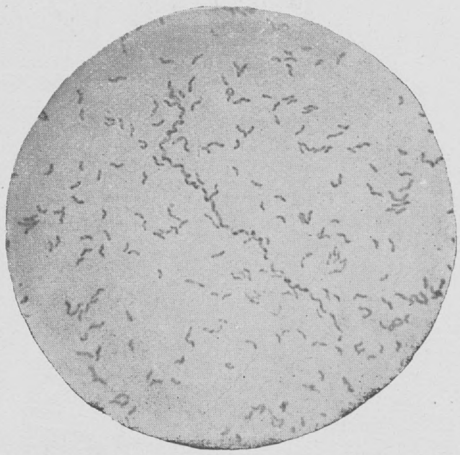
The two articles contained in this pamphlet, are based on papers read on the subjects of typhoid fever and cholera before the St. Louis Medical Society within the last few months. I have endeavored to put forth in bold relief the salient points involved without being dogmatic or schematic. I did not intend to write an exhaustive treatise on these diseases and left out, therefore, the technical features, simply stating or lightly touching upon what I have conceived to be the essential and most interesting points in the present status of our knowledge.

L. B.

The bacillus of Typhoid fever in the highest state of development (with moving filaments or flagella).
From a photograph by Riffarth, Berlin.



Vibrion (Spirillum) of Cholera. The corkscrew like thread traversing the center of the field shows the microbe in the highest form of its development.
Magnified 1000 x.
After Fraenkel and Pfeiffer.

TYPHOID FEVER IN THE LIGHT OF MODERN RESEARCH.

Introductory Remarks.— When, under the stimulus of the cell-doctrine, the pathological anatomy of typhoid fever had been settled to the satisfaction of the inquiring medical mind, a great step, and in the opinion of some, a final one, had been taken towards the understanding of the nature of that disease. Of course, there was still that intangible, mysterious something; the air and the soil in their varying conditions which baffled the investigators of those times and hovered over the minds of the hygienists and practical physicians as the Kismet does over the Turk. The pathological anatomy was well understood; but what was the ultimate cause of the histological changes peculiar to the lesions found in typhoid, and what gave rise to the variegated symptomatology of the disease? This was the question of questions, which engrossed the minds of the pathologists and epidemiologists of that period of medical history, which preceded the bacteriological era.

The enthusiasm which arose, not only in the medical laboratories but among the educated of the civilized world, in the spring-time of bacteriological research, in the beginning of the eighties, when, together with many other pathogenic microbes, the bacillus of typhoid fever was discovered, can be fully appreciated by those who, though in a modest way, participated in that movement and shared the hopes it awakened as to the reach and ken of the physician of the future.

Very naturally it was presumed that, once the causes being determined and located in these vastly preponderating diseases of afflicted humanity, the infections, it would be a step of less difficulty to find the agents endowed with the faculty of destroying those causes.

At that time it was considered a great triumph of progressive science to discover a new coccus or bacillus in a given infectious disease. The specific microbe having been determined, the next logical step was to seek out such chemical substances as were most incompatible with the lives of the several species of cocci and bacilli and thus to lay the foundation of the "only

rational'' method of treating infectious disease. The watchword: antibacterial therapy, was then heard for the first time.

Now, the hopes founded on this new departure gradually dwindled down; and, how the pessimists had in this, as in other matters generally, once more the better of the enthusiasts, I need not particularly emphasize, before a body of medical men, most of whom have watched with interest the developments in the history of our science during the last twelve years.

Practical tests showed that antibacterial therapy, with the sole exception of surgery, and, though to a lesser extent, dermatology, did not materially affect the results of treatment, and what was particularly discouraging to those that looked hopefully forward to a speedy achievement of cure and prevention in infectious diseases, was the fact that, by the mere finding of a specific and pathogenic bacterium, only a very slight advance had been made towards arriving at a knowledge of the true nature of the disease, especially to the manner of its spread, the channels of infection, the local and temporal conditions favoring or hampering and preventing its development, etc.

It was found that a bacterium, which, by common consent, had been recognized as the exclusive visible etiological factor of a given disease, was far from presenting the same morphological and biological characteristics, which their discoverers had established and described, and that the teaching of the oft insisted-on constancy of form, life-habits and pathogenic effect had to be considerably restricted in the course of time, with the broadening of the light shed by experiments and counter-experiments on these questions. Much that had been proclaimed as incontrovertible fact did not withstand the test in the crucible of clinical, respectively epidemiological observation.

The conviction had not, in those times, so firmly, as to-day, settled on the minds of investigators that what is true *in vitro* in the test-tube and the flask may not be true in nature.

The insufficiency of the results obtained so far in the laboratory, for the purpose of clearing up the heretofore mysterious features of infectious diseases, apply in a peculiarly forcible manner to the history of typhoid fever investigation of the past decade; but I hasten to add, that in spite of disappointments in some directions, there is perhaps no other disease where painstaking and untiring labor has met with such brilliant, scientific, and in some instances, surprising and eminently practical results.

Effect of Eberth's Discovery on Formerly Prevailing Notions. — After the bacillus, which now is recognized by the overwhelming majority of authorities as the exclusive morbific

agent in the typhoid fever process, had been discovered by Eberth,[1] Pettenkofer's theory[2] seemed to have been deprived of its mainstay, and the tide of clinical evidence tending to show the simply contagious nature of typhoid fever seemed to have gathered sufficient force to sweep off the grounds of scientific medicine a structure which had been erected and finished by untiring energy and wonderful ingenuity.

For years previous to Eberth's discovery clinicians, restive under the therapeutic, and, in a measure, prophylactic nihilism, which the prevailing epidemiological notions indirectly implied, had been at work to undermine Pettenkofer's edifice by the force of arguments based upon facts gathered at the bedside and in the surroundings of typhoid fever patients. The demonstration by Eberth of a bacillus found invariably in the organs most affected by the morbid process in every case of typhoid fever, seemed to furnish the missing link in the chain of those arguments.

Inadequacy of Bacterial Demonstration. — But the simple demonstration of a bacillus in all cases in which the clinical picture was that of unequivocal typhoid fever, though accounting satisfactorily for the pathogenesis of the disease as such, fell far short of explaining all the problems which in the course of the histories of epidemics had presented themselves for solution, and which since the discovery of the microbe were constantly multiplying.

Pettenkofer's Theory. — Above all, there was the remittent and intermittent character of the epidemics which called for a factor back of the bacillus and which seemed to be so felicitously furnished in the form of the hypothetical, local and temporal predisposition. After the germ, formerly only a logical postulate of Pettenkofer, had been found, it remained to be proven that under certain atmospheric conditions coupled with a low level of the ground water, the bacillus not only underwent a maturing process, necessary for a successful invasion of the human organism, but also that it was dispersed throughout the atmosphere, in order to reach its victims. This proof has never been furnished. Besides, many of the phenomena which formerly were utilized by Pettenkofer in favor of his theory have been interpreted by

[1] It is very questionable whether the one described previously by Klebs is identical with the one now regarded as specific.

[2] Cf. p. 20, article on Cholera.

modern observers in an opposite sense. It seems, therefore, that, as in cholera, so in the typhoid question one after the other of Pettenkofer's arguments have to yield to the doctrine of contagion as against that of the miasmatic origin of disease, in spite of the fact that bacteriology in its present state is still very far from explaining everything and that we are still in absolute darkness as regards some of the most vital points touching the question under discussion.

Morphology and Biology of the Typhoid Bacillus. — In order to have a proper appreciation of the difficulties barring the road to exact knowledge, but at the same time, of the palpable and demonstrable results which have been obtained through the study of Eberth's microbe, a short account of what we know of its forms and life habits may be in order at this place.

Polymorphism.—Unfortunately the most elementary of all criteria, its form, offers nothing characteristic. It looks like many other bacilli and, what is worse, varies very much according to the media on which it grows. This polymorphism it shares with many water-and ground-bacteria and with a number that are normal inhabitants of the intestinal tract. The one most frequently met with, and with which it is most apt to be confounded, is the *bacillus coli communis*. The ends are rounded off, so that a short specimen of the microbe may give the impression of an ovoid-shaped coccus. Under some conditions it develops seemingly into threads which on close inspection, however, are found to consist of a continuous chain of bacilli.

Motility.—Their motility is effected by vibratile cilia (flagella) of which the fully developed bacillus possesses from 3 to 6 or more. The larger individuals have a snake-like motion.

Nutrient Media as Affecting the Growth of the Microbe.—Like many other similar-looking bacilli, it grows in gelatine at ordinary temperatures, without liquefying it. Hitherto it has been held that its growth on potatoes is quite characteristic. But a close research has demonstrated that the thin, glistening, almost invisible film which covers the potato is produced by other bacteria likewise, and that, when the surface of the potato is rendered alkaline, a yellowish brown covering results. If to this uncertainty of the potato culture, which up to a short while ago was held to be absolutely diagnostic, is added the fact that Koch found 5 bacilli which in all respects are similar or even identical (excepting their pathogenic properties) to the typhoid germ,

and that Kitasato, a Japanese physician, and one of the ablest and most reliable observers of Koch's school, has a list of 16 different bacteria, all of which may be easily confounded with our microbe, it becomes intelligible, how perplexing the task may be of deciding the question: typhoid bacillus, or not, under certain conditions; when for instance, water or solid substances are to be examined for the typhoid germ. Of course, there is little difficulty in determining it, when the material for examination is taken from the living body or from one of the organs in which it is known to form colonies by preference.

Organs Harboring the Bacillus. — These organs are, besides Peyer's patches, the spleen, liver and mesenteric glands. Here the bacillus congregates and entrenches itself; only occasionally it is found in the blood. I myself have examined the blood of 6 patients without being able to demonstrate its presence either microscopically or by culture. By tapping the spleen with a hypodermic needle, it has been found by several investigators, in the blood thus obtained; as a diagnostic means, however, the spleen puncture does not, as a matter of course, recommend itself. Sometimes it occurs in the brain and spinal cord. One observer claims to have discovered it in the roseolar eruptions which, he says, are the results of bacterial capillary embolism. This observation has not been verified. In two cases which I examined, no bacilli could be demonstrated. More probably are the roseolar spots the results of toxic materials circulating in the blood.

Difficulties in the Way of Investigation. — But the chief difficulty barring a successful study of the typhoid bacillus lies in the utter absence of any animals spontaneously susceptible of the disease. Rabbits, guineapigs, rats and mice have been inoculated; in isolated instances the characteristic lesions in Peyer's patches were the result of such inoculations with pure cultures. But generally there was no infection, but merely a toxæmia[1] which rendered the animals sick or killed them. And it is not the typhoid bacillus alone, which possesses the power of producing both intoxication, and ulceration of Peyer's

[1] In a true infection the bacteria when introduced into an animal organism, develop and multiply, and the number of germs is, theoretically at least of no importance. A toxæmia will result secondarily from the poisonous products secreted by the pathogenic germs. In toxæmia, pure and simple, it is the amount of bacteria together with their poisonous secretions, that determines the result; absence of any effect, or intoxication followed, or not, by death. In toxæmia, then, the microbe may be found in the blood during life or after death; but it has been simply preserved, though perhaps in a viable state.

patches in animals. There are many ordinary water-and ground-bacteria that are not known as having pathogenous power, and yet yield the same result, when introduced into the circulation of animals.

It seems, however, that of late white mice have been successfully infected by some French experimenters. The introduction of typhoid bacilli direct into the duodenum analogously to Rietch's and Nicati's experiments with the cholera germ, seem to have been negative.

Variation in Virulency of the Bacillus.— Another great obstacle to obtaining uniform results is the changeableness of the virulence of the typhoid microbe. When bacteriology was still in its infancy the notion prevailed that there was not only a constancy of form but also a constancy of virulence in the various species of pathogenic and other bacteria. In fact, this was one of the fundamental doctrines in the new science. Pasteur was the first to do away with the latter error, and to-day there is nothing so well established, but at the same time so confusing and leading to contradictory results in experimenting, as the variability of microbian virulence.

The typhoid bacillus is no exception to the rule but may, on the contrary, be looked upon as a paradigma. Just as the cholera vibrion may be changed from an exceedingly poisonous, to a perfectly harmless state, and vice versa, so the typhoid germ is liable to acquire and lose pathogenous properties, by varying surrounding conditions.[1]

Influence of Light on the Microbe.— The sun-light especially, and the diffuse light in a less degree, are not only detrimental to its toxic properties, by enfeebling its growth, but they kill it in a short time. If, for instance, a number of test-tubes containing bouillon, sown with typhoid

[1] To make this unstableness of poisonous properties of the lowest forms of plants, the microbes, comprehensible, analogous examples in higher plants are generally adduced in the test-books on bacteriology. The bitter almond is in every respect like the sweet almond, and the bitter almond-tree has been shown to be the parent of the sweet variety, but there are the well-known poisonous properties of the bitter, which is the only difference between it and the sweet almond. Another example is found in foxglove. When Linnæus visited Lapland, he was astonished to see the natives eat this plant, made up as a salad. He ate of it himself and found that, what is regarded as one of the most poisonous plants in the moderate zone, especially in mountainous regions, is perfectly harmless and used as a vegetable in the extreme north. Perhaps the variability of typhoid fever epidemics as to morbility and mortality is to some extent attributable to the changeableness of virulence in the bacillus, although this is certainly not the only factor capable of explaining it.

germs, be exposed to the more or less direct rays of the sun, or kept in the shade, it will be found that the test-tube most directly exposed, does not contain any living specific bacteria any more, in from 3 to 6 hours after the exposure. It is not the heat, but, as has been proven, the chemical rays, that destroy the life of the bacteria. The diffuse day-light too, is inimical to its life and toxicity. Hence, it may be said, the typhoid bacillus shuns light and thrives in darkness, a powerful proof of the correctness of current notions as to the beneficial effects of sunlight and air, as enemies of disease.

Ectogenous Existence of the Bacillus. — Of the typhoid bacillus, as it occurs in nature, we have only a rudimentary knowledge. That it does exist in a saprophytic state, there can be very little doubt. Its faculty of thriving in ordinary temperatures and its unpretentiousness and, figuratively speaking, when compared with the cholera vibrion, its "sociability" with the ordinary saprophytes, enable it to accommodate itself to more or less adverse conditions. But where is its habitat? In the water or in the ground, where it leads a saprophytic existence with lessened or entirely suspended virulence? Is it a permanent resident in certain houses which are known as typhoid fever houses, and do the outbreaks of typhoid fever epidemics mean that the bacillus, favored by certain conditions, which we are at present unfamiliar with, has re-acquired its suspended or lost virulent character and is now ready to do its deadly work?

The answer to these questions cannot be definite as yet, but we can approximate the actual state of things by consulting the testimony as to the power of resistance under given conditions of the bacillus, as taught by the laboratory experiment and as epidemiological experience has recorded it.

Now, it is a peculiar fact, that in spite of its easy destructibility by the sun's rays, its vitality is astonishingly great under other seemingly most adverse and even fatal conditions.

Thus, it has been found that it will survive in ice for many months: an important lesson as regards the harmful practice of drinking ice water.[1]

[1] Here is a field of special interest to the boards of health of the larger and smaller cities of the country. There is a meat inspector and a milk inspector, but nobody cares where the ice comes from, provided it is stated by the dealer that he sells only "pure lake ice." Whoever has seen with what utter disregard to the simplest hygienic precautions the ice crop is gathered, must be astonished, if he be familiar with the fundamental teachings of bacteriology, that epidemic diseases are not of more frequent occurrence. I am sure that to the tumbler and the ice box are traceable many a case of typhoid and diphtheria. The ice box especially offers the greatest opportunities for food contamination.

Vitality of the Ghrm. — Alternate thawing and freezing, however, will kill it.

The results of experiments, as to the power of endurance in water, are rather conflicting. While one investigator (Karlinsky), who experimented on a large scale with cisterns out of actual use, found that ordinary water, contaminated with typhoid dejections, is devoid of bacilli in about 2 days, others have demonstrated that the germ can be kept alive in even impure water, for days and weeks.

Thus, it has been shown by laboratory experiment to live and thrive in Panke water (the Panke is a small creek which flows through Berlin and is about as notorious as Mill Creek or River des Peres are with us). Stagnant water offers more favorable conditions then flowing water; but even in the latter it will accommodate itself to adverse conditions.[1]

The Bacillus Found in Drinking Water. — Thus the bacillus has been found in the Seine water; during an epidemic in Iron Mountain, Michigan, Vaughn and Novy demonstrated its presence in the drinking water. In some other epidemics the search has been reported as successful. I myself had an opportunity of examining the water in two wells reputed to be infected. But the results of my examinations were negative. In both instance the specimens had been sent by express, offering thus an additional diffculty to the ordinarily existing ones, of arriving at a definite conclusion. [2]

But even with impure ice at our hands, the danger of infection may be greatly lessened by boiling the water, allow it to cool, and keep it in corked bottles *on* the ice. This diminishes, to say the least, the chances of introducing into the stomach pathogenic germs in heavy doses.

[1] I have been informed by a gentleman who passed through the late civil war, that a common method of purifying suspected water in the south was, to have it whipped with twigs for hours. At that time Liebig's ideas of oxygenation were still dominant. In the present light of bacteriologal science, the purification, which no doubt did result from the process of whipping, was due to the exposure of the bacteria to light, which renders almost all of them harmless, and of keeping them in motion, which prevents their multiplication and colonization.

[2] It is impossible to estimate the number of bacteria necessary for a successful infection and almost impossible to even approximately ascertain the number of pathogenic bacteria in drinking water. The ordinary manner of taking one or two drops or even ten or fifteen drops will commonly fail when the extreme state of dilution of the virus is considered, in which it must of needs occur in rivers. There may be one bacterium to a drop in a fluid to be examined, but there may also be one only to a litre, and the difficulty and unreliability especially as regards the presence or absence of the typhoid bacillus becomes at once apparent. Recently a centrifugal machine has been invented by Dr. Litten of Berlin, with which small particles of matter suspended in fluids, casts, urine, blood and pus-corpuscles, bacteria, etc., can be precipitated in a short time to the bottom of a test-tube. This instrument may be advan-

Epidemiological Proof.—The most conclusive proof, however, that river water may be the carrier and harborer of typhoid germs is furnished by the epidemiological histories of cities like Paris, Vienna and Berlin. In Paris it has been shown on different occasions that only in those parts of the city did the fever prevail in an epidemic form which were provided with Seine water, through the public works, whilst other parts deriving their supply from other sources were free. Vienna was a notorious typhoid fever city until the Danube water was replaced in the water works by a purer article from the mountains. A similiar experience to that of Paris had Berlin. Now, the presence of typhoid germs was neither demonstrated in the hydrant water of Vienna or Berlin, but the ceasing of the epidemics after changing the source of supply proved that the former supply was infected. In fact, water seems to be the chief disease carrier in epidemics of typhoid fever, whilst sporadic cases must be attributed to other channels of infection.

Durability of the Bacillus in the Dried State. — In feces and urine the typhoid bacillus has been found alive and pathogenic after months, a proof, to my mind, that the rôle of the grave-yard as disseminators of the fever cannot be dismissed abruptly, as has been done by several writers.

Its greatest durability is exhibited by the bacillus in the dried state. A silk thread drawn through a pure culture and dried will be found to contain virulent bacilli after twelve months.[1]

Dried feces are particularly tenacious as to virulence, and dangerous as to infection. The experience in Russian and German barracks have demonstrated it to a certainty. Most instructive is the history of an Hanoverian regiment, of which during the years '75-'84 no less than 45 per cent. were attacked with typhoid fever. Shortly after the discovery of the true cause of the disease, the specific microbe was looked for in the barracks and found in dried feces on some uniforms, which, according to the system of military service, had in turn been used by succeeding drafts of soldiers. The cleaning and thorough steaming of those uniforms stamped out that barrack epidemic; certainly one of the most conclusive proofs of a bacteriological truth and

tageously used in the examination of water for microbes. An electric fanmotor answers the purpose very well. By a trifling mechanical contrivance the Emerson motor whose speed can be regulated, is easily converted into a perfectly working centrifugal apparatus.

[1] Silk thread seems to possess a peculiar preserving power. Even the cholera vibrion, commonly so perishable in a dry state, can be preserved with its pathogenic properties for many months on silk thread.

one of the grandest triumphs of bacteriological research. Similar results, not less striking, were observed in Russia.

Portals of Entrance in the Body. — There is at the present day little doubt that the chief, if not the exclusive, portal of entrance of the typhoid germ is the intestinal tract. The lungs, formerly suspected under the dominion of the miasmatic theory, do not enter into consideration any more, as organs through which the poison gains access to the organism, except, perhaps, in so far, as noxious gases may, when inhaled, make an individual more susceptible of the infection. In other words, typhoid fever is not inhaled, but it is eaten and drank like cholera.

Soils Favoring Growth Outside the Human Body. — Like the cholera vibrion, the bacillus of typhoid fever thrives on all alimentary substances used by man. It grows on vegetables and meat. Milk, though spoiled, is a good growing medium and no doubt has carried typhoid fever into many a family. Butter[1] will preserve the bacillus for weeks. Seltzer water and probably a number of other artificial mineral waters offer it a place of refuge.

Circumstances Facilitating Invasion. — Of course, as in all diseases, there are collateral causes, favoring the development of the germ by preparing the soil, *i. e.*, weakening the human body. Such collateral causes are depressing conditions, but above all the physiological misery, the underfeeding and crowding together of people, neglects of simple hygienic laws, debauches, exposure, etc.

Incubation. — Supposing that the contagionist view (in a wider sense) is correct, and that typhoid fever cannot arise in persons who have not in some way introduced the specific bacterium into their intestines, the question presents itself: How long a time is requisite for the parasite to multiply and colonize, before the clinical symptoms make their appearance? The general impression, founded upon the records of cases imported into previously uninfected communities, has been that the interval between the presumed infection and the demonstrable beginning of the clinical symptoms is about 3 or 4 weeks. Almost conclusive on this point is an observation made by Dr. Almquist, a Swedish physician and a recognized authority in the epidemiology of

[1] Of late " infected " butter has repeatedly received the attention of hygienists.

typhoid fever: A servant girl returned from her service to her village, sick with typhoid. No case of this disease had existed in the village at the time of or previous to, her arrival. In 3 to 4 weeks the whole of her family was taken with the fever.

Mixed Infections. — The typhoid virus gives rise to a multiplicity of lesions. No organ or tissue is safe from its deleterious action. The coarse changes, however, witnessed in the course of the disease, and after it, are generally due to a fresh infection with other micro-organisms. Chief among these are the pus-producers. When the typhoid bacillus is doing its deleterious work these microbes have a better chance of invading the body of the patient. The ulcers, notably those of the larnyx and the abcesses which are not unfrequently met with, are the results of these secondary invaders, principally the staphylococcus pyogenes. Occasionally, though, the bacillus of typhoid fever has been found to possess pyogenetic properties.

This raises the question, whether other lesions complicating the disease may be the work of the typhoid microbe exclusively or whether additional invaders are requisite to produce complicating disorders. Thus, pneumonia supervening in the course of the malady or erysipelas, have been contended by some to be caused by the typhoid bacillus, whereas other observers have maintained that these complications are caused by the respective micro-organism peculiar to pneumonia or erysipelas.

The pneumonias complicating typhoid, which I had an opportunity to examine microscopically (a few by culture) showed pneumococcus in a few instances and a streptococcus-infection in others. In some I found the typhoid bacillus, in one case alone, in others in conjunction with Weichselbaum-Fraenkel's diplococcus. What is termed typho-pneumonia is etiologically speaking a diplococcus infection and has nothing in common with typhoid fever. Pneumonia occurring during typhoid is, as a rule, a mixed infection [1]

The same is true of erysipelas developing during the disease. Here the streptococcus can generally be demonstrated.[2]

[1] Hypostatic pneumonia is to be strictly separated from the infectious forms. Its origin is a mechanical one; its primary cause being an insufficiency of propelling power on the part of the heart.

[2] Erysipelas, though, as ordinarily understood, a pathological entity, the etiological factor (streptococcus), being always the same, was by some, thought to be merely a manifestation of the activity of the typhoid bacillus, when appearing in the course of typhoid fever. It was logically inferred that a germ which was capable of producing inflammatory processes in the intestines might under certain conditions localize in the skin, giving rise to a dermatitis which, clinically considered, it would be impossible to distinguish from typical

Typho-Malaria. — The question of typho-malaria has for decades, since our civil war, during which nearly 5,800 cases occured in the Union Army, agitated the mind of the clinician, especially the general practitioner. Clinically we understand by typho-malarial fever a modification of typical typhoid characterized by pronounced remittence or even intermittence of the febrile movement, at the beginning or at the decline of the process. It was assumed that the miasms which were supposed to be at the bottom of malarial fever possessed this modifying influence on typhoid fever when occurring in malarial countries, and that, according as the malaria or the typhoid symptoms showed themselves first, there was a malarial fever complicated with typhoid, and a typhoid complicated with malaria. Others again assumed typhoid-malaria to be a hybrid entity, in the sense of resembling both, but being neither one nor the other.

What clinical observation alone has been notoriously unable to elucidate (for the subject of typho-malaria is as muddled to-day as it was during the civil war), the microscope will probably be called upon to settle. The matter presents itself in this simple form: Are there cases in which besides the typhoid bacillus and the anatomical lesions peculiar to typhoid fever, the plasmodium malariæ is found in the blood? And, furthermore, is there a disease in which the plasmodium malariæ can be demonstrated in the beginning and Eberth's bacillus later on, and vice versa?

Although the notion was quite prevalent in former theorizing times, that one specific infection excluded every other, it is now a well-established fact that two or more different kinds of parasites may be found in the same host, or in bacteriological parlance there is such a thing as a symibiosis or mixed infection; and there is *a priori* no valid ground to object to the presumption of the plasmodium malariæ inhabiting the human body in harmony with the bacilli of Eberth. To my knowledge this has up to the present time not yet been demonstrated. In five cases of what was clinically regarded as typho-malaria my blood examinations were negative; the plasmodium was not found.

Atypical Localization. — The appearance of a pneumonia in one or another of the etiological (streptococcus or diplococcus in-

erysipelas. Hence the typhoid bacillus was looked for in such cases, but excepting one or two observations, was not found, a streptococcus being generally met with. That, however, an osteitis, periosteitis, and abscesses in parts distant from the topical intestinal lesions may be due to the typhoid bacillus, has been repeatedly demonstrated. But more frequently the staphylo- and streptococcus have been encountered in such instances as secondary invaders.

fections, *e. g.*), and anatomo-pathological (fibrinous or cellular) varieties, has been animadverted to in another place; the atypical localization of the typhoid process in tissues and organs other than the glands of the intestinal tract, has likewise been alluded to. But there is another subject closely related to the preceding one, on which considerable darkness and confusion reigns — I mean the question of typho-pneumonia considered as a disease, *per se*.[1] When in a given case pneumonia assumes a "typhoid" character, *i. e.*, when there is a dry and brown tongue, sordes on teeth and lips, low, muttering delirium, great prostration, tremor and subsultus tendinum, etc., the diagnosis, typho-pneumonia, is readily made. Here, then, too, the momentous question arises: Is this form of pneumonia one in which, in the course of an ordinary pneumonia, that rather mythical and nebulous element, "typhoid condition" supervenes, or is it a case of mixed pneumococcus and typho-bacillary infection, or lastly, is the pneumonia due to an atypical localization, in consequence of which the intestinal symptoms are either minimal or do not exist at all, and where consequently the pneumonic process of typho-bacillary origin is in the foreground of the clinical picture?

There can be no doubt as to the occurrence of cases belonging to the last named category and which cannot be interpreted otherwise than by the assumption either of a symbiosis of the two specific microbes referred to above or of an atypical localization of the typhoid bacillus which, causing primarily an inflammatory process in the lungs, invites and prepares the soil for the diplococcus pneumoniæ as a secondary invader. I stated above that in one case of pneumo-typhoid, I found Eberth's bacillus alone. This was a case of the ambulant variety. The lung was not solidified, but was in a state of splenization. The intestinal lesions were exceedingly insignificant and were those met with in the first week of typhoid fever. Possibly such cases are not so rare as reports obtained so far would lead us to believe, the difficulty of getting exact data on this point being caused by the fact that cases dead with typhoid come to the autopsy table as a rule after the earlier stages of the disease are passed. From the expectoration in the early stages of pneumonia in typhoid, the specific bacilli may indeed be obtained by culture, but the diplococci are always present alongside with them and vastly preponderate in number. Owing to the bronchial catarrh, which perhaps is present in every case of typhoid during the first week, and the

[1] Analogous to typho-pneumonia, and involving the same problem, is typho-nephritis, or nephro-typhoid, which I leave out of consideration because the questions of principles and essentials comprised are the same in this as in the first named.

secretions of which almost invariably contain the diplococcus, wherever and whenever the catarrh exists, the diagnostic value of the sputum is very limited.

Reverting to the cases of typho-pneumonia or what is ordinarily understood by that name among practitioners, I would say that the question is not yet ripe for final adjudication. When such cases occur during typhoid epidemics they may reasonably be set down as real typhoid with atypical localization in the lungs, the specific bacillus being aided and re-inforced by the diplococcus pneumoniæ. If, on the contrary, they are observed outside of a typhoid epidemy the inference must be that the diplococcus pneumoniæ (perhaps a streptococcus), instead of colonizing in the lungs, pervades the whole organism, setting up a blood-infection, as is witnessed in the animal experiment, where inoculations with the germs peculiar to pneumonias, do not have a tendency to localize, but pervade the whole body indiscriminately.

Latent Microbism. — In connection with the preceding remarks it is perhaps appropriate to cast a glance at the theory of "Latent Microbism," as enunciated by Verneuil. According to this observer a person may be infected without being actively attacked by the disease, that is, the germs may simply camp and entrench themselves in certain organs of the body, waiting, as it were, for a favorable opportunity to break out and attack the organism, as soon as it is in the proper, *i. e.*, weakened condition, promising in a coming combat, a victorious issue. As may be seen, this is rather a phantastic way of dealing with a pathological subject, but the thing itself is not impossible. In pneumonia and erysipelas, for instance, latent microbism has been proven almost to certainty.[1] Possibly a similar state of affairs obtains in the genesis of typhoid fever.

[1] The former often developes in a remarkably short time after a severe cold or a trauma. So short indeed is sometimes the interval between the obviously immediate cause and the outbreak of the disease, that the inference of a concomitant bacterial invasion is highly improbable. The assumption that, as in the mouth, so in the lungs there may lie pneumococci in a dormant, *i. e.*, non proliferating or harmless state, a state which is at once changed by a weakening of the surrounding cells, explains the apparent discrepancy. In some cases of erysipelas we have likewise a rather cogent proof favoring the theory of "Latent Microbism." In fresh cases as well as relapses we are constrained to assume the latent presence of the streptococcus, which enters upon an active stage, as soon as the surrounding cells weakened by trauma, cold or other noxious agents permit of it. My own conviction is that the anxiom formerly held in regard to syphilis; once syphilitic, always syphilitic, is certainly true of some cases of erysipelas. Once erysipelatous, always erysipelatous! This means that the so-called predisposition to this disease after an attack consist in reality only in a number of relapses brought about in the manner indicated above. It is my opinion, based on clinical and bacteriological evidence, that

Antispecific Views. — I cannot pass with silence the antispecific views which are still entertained in some quarters in spite of exact scientific evidence of bacterial etiology. The exclusive theory of "atmospheric and telluric influences" so much dwelt upon by the writers and teachers of a past period has still its adherents and faithful devotees.

Others still hold to Murchison's views, which at one time commanded the attention of the medical profession. According to Murchison, any kind of organic matter, but especially fecal substances, when undergoing an abnormal fermentation, are thought to be capable of giving rise to typhoid fever.

Another class again, with Dr. Peter, the celebrated Paris clinician, at the head, speak of an auto-typhisation, which is perhaps somewhat more in accord with modern pathological views. The poison, in the opinion of Peter, is generated in the body through a faulty metabolism, in a manner similar to the much talked of auto-intoxications.

Lastly, Rodet and Roux, likewise French investigators, maintain that the *bacillus coli communis*, an harmless inhabitant of the intestines of healthy individuals, has the faculty of being converted under abnormal conditions into the genuine and poisonous typhoid microbe, so that every person carries, so to speak, the germs of a prospective typhoid fever with him.

The upholders of all these views stand, however, rather isolated among the authorities of our profession of to-day.

Typho-toxines and Toxalbumines.— As in all infectious diseases, as soon as their specific parasite had been discovered, so in typhoid fever the cause of the symptoms, above all that producing fever and stupor, was sought after in the form of some essential, active principle. At a comparatively early stage in the development of bacteriology it was correctly surmised that it could not be the bacteria themselves, but that it was the secretions, to which must be attributed the various symptoms of poisonings, presenting themselves in the course of the infection. At first it was supposed that substances similiar to the alkaloids of medicinal plants, were causing the fever, convulsions, stupor, etc., peculiar to the several diseases. The typhotoxine was one of the first of such hypothetical alkaloidlike

the streptococcus causing erysipelas may be dormant in the previously infected body for years, before under favoring circumstances the relapse occurs, a relapse which may, it is true, appear under a clinical form differing from the original malady, attacking deeper tissues and organs. Such cases have, time and again, been adduced as irreconcilable with bacteriological teaching, whilst in reality they are among the strongest proofs of the microbian doctrine.

substances produced. The fact is that it made *some* symptoms of typhoid, when incorporated in animals, but not all. Probably a variety of toxic substances is at the bottom of the symptoms in typhoid, as in other infectious diseases. This question is, however, also far from settled yet. Of late it is not the toxines but the toxalbumines which are thought to be those essential, active principles.

Chemical Explanations of Immunity. — There is a curious experiment first published by Widal and afterwards verified by some other experimenters which, perhaps, some day will throw light on the vexed question of immunity. It is as follows: If, on a gelatine plate, typhoid bacilli are planted and these develop into colonies, and these colonies be lifted off by steralized platina needles, it will be found that any attempt at growing another crop of typhoid bacilli on that same gelatine will fail. In other words, it is immune from the typhoid bacterium. The inference to be drawn from this experiment, is almost too obvious as to be specially stated. If we mentally substitute the human body for the gelatine, we have the conception of immunity, in a tangible form, and its mechanism becomes comprehensible. Either, there is something wanting in that gelatine which to the development of the typhoid bacillus is essential, but which one crop of bacilli has already used up, or the colonies have deposited a substance which prevents a future growth of the same kind of bacteria. Here, then, we have *in concreto* the two views of immunity, which for years were struggling for supremacy, the doctrine of addition and that of subtraction or exhaustion. Pasteur was, and is probably still, a partisan of the former view first enunciated by Klebs, viz.: that immunity means the addition or incorporation of some substance which acts as a poison to the several invading pathogenic microbes. Unfortunately the question of immunity is a very complicated one and things take place in the living body in a manner vastly differing from that which occurs in dead gelatine.

Nor are the other theories of the immunity question more likely than the preceding one, to lift the veil of obscurity from this tangled subject.

Phagocytism. — The most plausible of these theories, and one which for several years has had many adherents among medical men, is that of phagocytism. A few words about this, as far as it applies to typhoid fever, may not be out of place. According to this ingenius conception of one of the ablest of living bacteriologists, Metschnikoff, immunity means the capability of

the leucocytes, which are compared to soldiers, of successfully coping with an invading army of pathogenic bacteria, or in other words, robust health and ample digestive powers of the leucocytes are equivalent to immunity from infectious disease. For the vigorous leucocytes (called phagocytes because of their devouring capabilities) not only eat the invaders, but also digest them. But however true this may be of other bacteria, no typhoid bacillus has as yet been found in a cell like as in anthrax, which has furnished the basis for the doctrine. The typhoid bacillus always lies between the cells. This is at any rate the unanimous testimony of competent investigators. If, however, phagocytism were applicable to the question of typhoid fever, we would be in possession of a satisfactory explanation of the fact that so many persons get fat and are in better health after recovery from typhoid fever than they were before. The phagocytes, namely, when successful (after they have rallied owing to the bacteria having become weak in their own poisonous secretions) not only eat the invaders, but also the remnants of their own dead comrades and brothers, and all the debris of the battlefield. This general cleaning up is said to confer on some convalescents an exceptionally good state of health.

As may be gathered from the foregoing, many perplexing questions still cloud our knowledge of the true nature of typhoid fever and of the great mass of the other infectious diseases. Our stock of undisputed facts on this subject is still small considering the vastness of the material; for, bacteriology is as yet in its swaddling clothes. May the physician of the future be in the same position to the bacteriologist of to-day, as the electrician of to-day is to Galvani, whose discovery, though only of theoretical import at the time, was destined to change the face of the globe.

FACTS AND DOUBTS ABOUT CHOLERA.

One should think that, the etiology of cholera being settled beyond cavil, and the unity and specificity of its organized virus being firmly established, it would not be difficult to arrive at harmonious conclusions as to the manner in which it spreads and the means best calculated to prevent it from becoming epidemic.

The cholera vibrion is, indeed, today the best known of all bacteria, and its biological properties have been so assiduously studied by a large number of competent investigators, that it seems strange that there should prevail so much difference of opinion even on the most fundamental and elementary points bearing on the cholera question.

This divergence obtains even on facts evolved by laboratory experiments, and when a definite and uniform conclusion has been reached in the laboratory, it is often difficult and in some respects impossible to make the experience, gathered under artificial conditions, to tally with certain phenomena presented by the disease itself. This discrepancy between experiment and disease is in keeping with what is ordinarily observed in the theory and practice of medicine, viz.: That the experiments performed by man are in most instances as yet poor counterfeits of those made by Nature herself.

Still, the laboratory experiment, crude and incomplete as it may seem, when compared with the complicated and often hidden and quasi-mysterious manifestations of Nature's workings, is in our present state of knowledge the touch-stone capable of enlightening us on that which is essential and that which is incidental and indifferent in disease, and thus preparing and clearing the road for exact knowledge and correct and efficient action based thereon.

This being admitted, the discrepancy just alluded to is rather discouraging to the friend of rational, exact and progressive medicine. Thus, it seemed to be established, beyond the shadow of a doubt, that in Koch's cholera vibrion the exclusive and specific bacterium had been found. If, however, the observation of Cunningham, who studied cholera in its home in India, are correct, there are at least ten different spirilla well differentiated by certain biological characteristics, all of them met with in the intestines of cholera patients, and, what is more, there are cases of cholera without any spirilla.

This announcement is so startling because entirely subversive of the very foundations upon which the modern doctrine of the cholera question has been erected, that for the present its correctness may well be doubted, because it is at irreconcilable variance with the results of the investigations of all other trustworthy observers.

The unity and specificity of the cholera virus is to-day at least as firmly settled as that of tuberculosis or anthrax, but this virus is not the comma bacillus, as it is still currently stated, but the cholera vibrion, or, still more exact, the cholera spirillum.

When Koch first discovered it he formed his conclusion as to the etiology of cholera on the appearances of the microbe as found in the dejections of cholera patients and on cultures obtained in gelatine. Later researches showed, however, that the comma form represents only the fragments of a maturer phase of development, which is spiral in shape, hence called spirillum or, from its wriggling motion, by the older name of vibrion. This spiral form of development, often presenting long filaments, is best obtained in bouillon-cultures.

The other competitors of the now universally recognized specific cholera microbe, Finkler's and Prior's vibrion, and the so-called Neapolitan bacillus, had to yield their aspirations to ætiological dignity and may now be considered to be definitely disposed of as pathogenic factors in cholera. The different biological behavior of Miller's comma bacillus as a normal inhabitant of the mouth and that discovered by Deneke in cheese, have long since been proven to be too distinct in their biological behavior from Koch's microbe as to deserve any extended discussion.

For a long time, the doctrine that the lungs were the portals through which the virus found entrance into the organism in all epidemic diseases counted the greatest number of adherents. The pathogenetic role of the "miasmata" was founded on this hypothesis. Thus it was thought that, as the poison of typhoid entering through the lungs, localized in the lower part of the ileum, and that of variola entering through the same portal, had a selective affinity for the skin, so cholera was also inhaled, selecting the upper part of the small intestines for its local manifestations. A direct inoculation through the blood in the manner of diphtheria, which, finding access through a solution of continuity of the skin, produces by preference local lesions in the fauces or larynx, was perhaps not much taken into consideration, although the former classification of cholera as a contagio-miasmatic disease would point in that direction. In the present state of knowledge only one mode of entrance can be admitted; this is through

the intestinal tract. For the blood, through which the cholera vibrion would have to pass before colonizing in the small intestines, does not, according to experiment and post-mortem finding, offer the necessary conditions for its maintenance and proliferation; the living blood is poison to the cholera microbe; it kills it.

Supposing now, that the cholera microbe, in order to gain access to the upper part of the small intestines, *i. e.*, that part of the human organism where it finds all the conditions favorable to its development, has for its exclusive portal of entrance the alimentary tract, that, in other words, it is eaten or drank, where do the disease and death-producing organisms come from?

This question brings us face to face with the momentous controversy, which immediately on the discovery of the cholera vibrion divided the reigning authorities into two camps. Up to the time of Koch's discovery and the conclusions he based on it, Pettenkofer's theory of the local and temporal disposition as being indispensable to the existence of an epidemic, had reigned supreme in the medical world. Pettenkofer himself had postulated the existence of a parasite which alone could explain the fact that the masses of the population were stricken with the disease. But in contradistinction to Koch, who, on the strength of his observations, claimed that the specific vibrion, as it is passed with the dejections of cholera patients, was itself sufficient to set up the disease after gaining access to the intestinal tract of a predisposed individual. Pettenkofer, baeked by statistical material covering a number of former epidemics, and collected with a wonderful amount of industry and ingenuity, maintained that the parasite, in order to develop its deleterious and poisonous properties, had to undergo a sort of maturing process in the soil, and that to this end a porous, permeable soil, rich in humus, and a certain temperature were necessary to the production of an epidemic. This was the famous local and temporal disposition alluded to above. In order to elucidate and make plausible his theory, he called to his aid the best known and most firmly established fact in all mycology, the analogon of sacharine fermentation, investing it at the same time with a mathematical formula. The yeast plant (x), he said, needs a solution of sugar (y), in order to give rise to a product, alcohol (z). In the same manner the cholera vibrion (x) needs a proper soil (y) to produce the disease, cholera (z). Whether his observations on the rise and fall of the groundwater always corresponding with the rise and fall of the morbility and mortality of the prevailing epidemic, will be verified and amplified in future epidemics, or whether the apparent causal connection between the two will be shown to be a mere coincidence, although a very curious and strik-

ing one, is a matter of great interest and importance. For the present the "contagonists and drinking-water theorists," as Pettenkofer dubbed the followers of Koch's doctrine, have the upper hand in this controversy, and the experiences gathered so far in the present epidemic do not tend to strengthen Pettenkofer's position. True, there is still a disposition on the part of the friends, and it must be said even on that of some of the followers of the new school, to reconcile the soil-theory with that of contagion, but to the impartial peruser of the literature on the subject these attempts seem like a sort of reaction following the great bitterness and animosity which have marked the controversies of the past on this subject.

It speaks well for the hearts of these savants to let the father of scientific epidemiology down easy, after it has been demonstrated to well nigh a certainity that he was on the wrong track, a track on which, however, he did remarkable and faithful work.

Foremost of these mediators is Hueppe, one of the most eminent and industrious bacteriologists of our time. Hueppe claims to have discovered, contrary to Koch and his immediate followers' assertions, that under certain conditions sporulation takes place in the cholera microbe, and that consequently a possibility of the parasite to live and proliferate outside the human body exists. This exogenous formation of the cholera virus as opposed to the exclusively endogenous one, as taught by Koch, is indeed, the *sine qua non* of Pettenkofer's doctrine. Admitted, that the parasite which bacteriology had so far shown to be extremely delicate and vulnerable outside of the human body, could under certain conditions live and multiply in the soil, that, in other words, instead of being a strict parasite it could live like ordinary bacteria of putrefaction, and lead a saprophytic existence, a powerful prop to the tottering edifice of Pettenkofer's doctrine would have been furnished.

Such lasting spores, now, similar to those of the anthrax bacillus, able to withstand all kinds of deleterious influences, and waiting only to be incorporated in the human organism, in order to develop and set up the dread disease, are said to have been observed by Hueppe. Supposing then that the cholera vibrion is accidentally sown in congenial soil, *i. e.*, porous and rich in humus, that a favorable temperature exists, that the groundwater recedes, leaving only a so-called evaporation-zone furnishing the necessary amount of moisture to the microbe, all the requisite conditions for an epidemic will be there. The spores will be communicated to the surrounding atmosphere, will gain access to the alimentary tract of mankind and an epidemic results.

The existence of these spores is, however, strenuously denied by nearly all other competent investigators, and all experiments to cultivate the cholera vibrion in the ground have failed. No matter in what quantity or in what state of development or virulence the microbe is committed to the soil, in one or two days there is no trace of it left. Therefore, although epidemicologically Pettenkofer's teaching may seem plausible enough, biologically there are very many arguments against it.

These leads us to the pivotal point of the whole question, viz.: the biological properties of the cholera vibrion.

Koch has found that this microbe was extremely pretentious in its life-habits, and required a number of congenial conditions in order to maintain itself outside the body. Thus, a slight degree of acidity, dryness, and above all the presence of other bacteria, would hamper or prevent its growth. Owing to this pretentiousness in its life-habits some epidemiological facts could be explained, while others refused to be reconciled with the results of biological research.

According to the concurring testimony of all observers, the cholera vibrion, in order to thrive outside of the human body, requires plenty of oxygen; it is an aerobe. When planted, for instance, in water, it will rise to the surface and form a film, whereas, in the depths of the fluid no trace of it can be discovered. The supply of oxygen, however, although it increases the resisting power of the microbe, lessens its virulence. Hence the often observed fact, that after a few generations in gelatine or on other cultivating media the cholera vibrion has lost all its pathogenic properties and has degenerated into a harmless saprophyte. The virulency, however, may be re-established by placing it under conditions similiar to those that prevail in the intestines.

If, e. g., a pure culture which has lost all trace of virulence, be planted in an egg through a fine aperture made in the shell, the hole sealed up and the egg be placed in a brooding oven, that is, if the anaerobic conditions, the soil and the warmth be approximately reproduced that prevail in the small intestines, where the vibrion develops its highly poisonous properties, an extremely virulent microbe results which, however, is also remarkably perishable. This is Hueppe's experiment, whose importance cannot be over-estimated. It teaches that, whereas the free access of air facilitates the growth of the microbe and its resisting power, by providing it with a protecting membrane, deprivation of air tends to increase its virulence, but enfeebles its power of vitality.

Koch teaches that the cholera vibrion is an hydrophilous bac-

terium, that the danger of epidemics lies in infected water courses. Now, it is a fact, denied by no one, that the cholera vibrion thrives only in sterilized water, *i. e.*, where there is no competition of other bacteria; that in the struggle for existence with all the known saprophytes our microbe succumbs and disappears from the field of competition in the same ratio as other microbes abound. This is true of water, of the soil and other substances harboring micro-organisms. In feces, for instance, unless sterilized, and urine, especially when decomposing, the cholera vibrion speedily dies. It is an aristocrat among the bacteria. The more dirt, the greater the stench, the surer the annihilation of one vibrion.

The worst, the most certainly germicide surroundings are a mixture of decomposing feces and urine. It kills the cholera germ as surely as the most powerful antiseptic.

In the face of such facts yielded by rigid and exact experiments, it is amusing when one reads of reports that such and such a place is fairly "reeking" with bacteria, and that it forms a dangerous brooding ground for the cholera microbe, should that disease ever take a foothold. Paradoxical though it may seem, such places would, in the light of strict experiment, seem cholera-proof, for whenever there is stench from putrefaction there are the saprophytes, the cause of decomposition, and there are the implacable and invariably victorious enemies of the cholera vibrion.

Dirt, then, and filth, the reputed allies, and, according to some, the originators of cholera, might, in the light of experimental research, be considered as the friends of humanity, because they are the foes of the cholera vibrion.

How does this compare with clinical and epidemiological experience? It certainly is true that where there is most dirt and filth there is also the greatest harvest of cholera epidemics. But it is equally true that where there is most squalor there is generally the greatest crowding of people in narrow rooms, the greatest facility of personal contact and the least resisting human organisms owing to hunger, exposure, disease, debauch, etc. It is not the soil, then, that breeds the disease germs, although this possibility must still be admitted and remain an open question, but it is the personal contact, the transferring of the pathogenic microbe by soiled clothing and unclean hands, to drinking and eating vessels or the fluid and solid aliments themselves. How else could the ship epidemics be explained that we have recently witnessed, or the tragic fate which several weeks ago overtook a wealthy English family, consisting of five, in Paris, all of whom died of cholera within a few days?

That cleanliness, not only personal, but also public, will still be the chief safeguard against the approaching foe, is too much a matter of course to deserve more than passing notice. But this cleanliness must be of the sterilizing kind, and must not be confined to the body and its clothing, but also to what we eat, and especially what we drink.

Now, all the ordinary foods in the raw or boiled state, provided they have no acid reaction, are favorable cultivating grounds to the cholera-vibrion, even the boiled potato, in spite of its acidity. Very naturally the attention of investigators has been particularly directed to milk, the recognized and most dangerous of all disease-carriers. Here again the paradox presents itself, that slightly spoiled milk does not offer the vibrion any chance of taking a foothold because other bacteria have already taken possession, killing the new-comer on its first appearance. Only quite fresh and unadulterated milk offers our vibrion a chance to produce its like. One more proof that this microbe requires everything of the cleanest and best to thrive!

If, now, this germ is so very particular as regards the company of less exclusive micro-organisms, how is it that rivers can be declared infected as have been done of late in Germany? Certainly, in order to make such a declaration, specific vibrions must have been found in these rivers, which, flowing as they do through great centers of population, are not lacking in ordinary putrefaction bacteria, the foes of the cholera germ? And did the much talked of and often quoted tank in India, which swarmed with cholera microbes, in which the natives washed their linen and out of which they drank in turn, did it contain the vibrion in pure culture? Common sense speaks against such an assumption. Hence we must conclude that the laboratory experiment is once more at variance with that performed by nature.

In view, then, of so many and vital contradictions, what is there of a positive nature in the cholera question? Above all, has it ever been proven peradventure that cholera can be communicated by contact, or that it can be eaten or drunk? We have just witnessed the clownish spectacle of a reporter in Hamburg who willfully sought the danger of contact and of drinking infected water, with a view of proving that he was cholera-proof, owing to an anti-cholera inoculation.

Before him, a foolhardy Frenchman, Bochefontaine, swallowed pills made of feces of cholera patients, and Klein, who ought to have known better, did the same in Bombay. None of them were attacked by the disease. What did this prove? If anything, perhaps the long-known fact that fools are under the special guardianship of Providence.

Nor did the isolated case of cholera infection from a pure culture, occurring in Koch's laboratory, when there was not a single case in all Germany, prove the communicability of the disease by pure culture. Such questions are settled by hundreds and thousands of cases, but not by one or two.

The great obstacle in the way of gaining definite and incontrovertible knowledge on this point is, that there is no animal which either spontaneously or artificially can be said to be attacked with true Asiatic cholera, and that, therefore, the most important link of the chain of evidence as formulated by Koch, for the demonstration of specific bacteria, namely, the production at will of an infectious disease by a pure culture of the respective bacterium, is still missing in the study of cholera.

The experiments performed so far have, it must be admitted, yielded results, recalling in a measure choleraic infection in guinea pigs and dogs, for instance, but the conditions under which the disease, *i. e.*, a violent intestinal catarrh with copious serous exudation, took place in animals experimented upon, bore no resemblance to those conditions under which cholera takes place in man. If, for example, the intestine of an animal is first bruised, or the common bile duct is tied, or opium is administered, or large quantities of alcohol ingested, or the stomach is rendered alkaline, before introducing the cholera virus, it is clear, that these are conditions which differ widely from those that nature presents, and, whether successful or unsuccessful, such experiments are only of relative and conditional value, especially since other bacteria beside the cholera microbe have been demonstrated to possess the same deleterious action on the animals under like conditions.

Our chief source, then, of information about the cholera process will be, as heretofore, clinical and anatomo-pathological evidence. And what does this teach? The symptoms, as well as the post-mortem finding, point to an intense poisoning process. Indeed, unless an epidemy is plainly established, it is very difficult, and often impossible, to make a differential diagnosis between the symptomatology and, I have no doubt under certain conditions, even the morbid anatomy, of poisoning by arsenic, *e. g.*, and other substances, without a concomitant bacteriological examination. The only man capable of diagnosing positively a case of cholera when he sees it, and to whom bacteriology seems to be a superfluous adornment to medicine, is a "cholera expert" at present in the service of the government. If the papers have correctly reported, he deemed a bacteriological examination useless, after *he* had made the clinical diagnosis.

To revert to our subject. The resemblance to a poisoning process is due, according to Koch, and most of the modern observers, to a specific putrefaction process in the upper part of the small intestines, the chemical product of which has the power of causing, when absorbed into the circulation, the dreaded and notorious nerve symptoms, and anatomically producing a necrosis of the epithelia of the intestines as well as those of the secretory organs, especially the kidneys, in consequence of which anuria results. Some, however, believe that the grave nervous symptoms are not caused by any cholera toxines, generated as metabolic products by the specific bacteria, but that those symptoms are due to inspissation of the blood by the excessive loss of water, the blood retaining all the offal products generated by the fever and ordinary wear and tear of the body, whilst still others are of the opinion that the cadavers of the cholera vibrions, respectively their decomposition and the absorption of the products of this decomposition, are responsible for the symptoms of the choleraic attack.

Very naturally, a number of investigators went to work to extract and isolate the supposed poisonous substance. The results have been far from harmonious, which perhaps is due to the fact that the bodies purported to be cholera toxine were obtained under different conditions of virulence; some, no doubt, from the absolutely harmless microbes that had grown in a liberal supply of oxygen. All of the toxines, however, obtained by the various experiments, Brieger, Villier, Pouchet, Klebs and others, produced, when injected into animals some, not all, of the symptoms of cholera, principally, paralysis and tremor. There is, however, at present, too much discrepancy in the results, as to attach any great importance to any of them, and although poisonous substances have been obtained from cholera vibrions cultivated in eggs with the above mentioned result, increased virulence, it cannot be said that the cholera toxine has been discovered. Here, too, science is still in the dark.

I have in the preceding remarks touched only a few of the mooted points in the cholera question. Of course there are a great many more, and the farther science advances and the deeper the human mind penetrates into the mysteries of Nature's workshop, the more riddles will present themselves for solution in this as in other branches of the natural sciences.

In consideration of these many harassing doubts and balking uncertainties, it is refreshing to see how some writers inside and outside the profession, especially the latter, seem to know all about cholera, even its prevention and cure. The charming positiveness with which such authorities as Edwin Arnold pronounce

themselves about the effects of quarantine and hydrochloric acid is quite a relief from the depressing consciousness of the often mentioned doubts and uncertainties. Unfortunately it is only the most ignorant in medical, as in other matters, that are the most positive in their assertions; and literateurs in particular have, ever since the illustrious examples were set by such men as Goethe and Carlyle, the uncontrollable impulse, when giving their opinion of medicine and doctors, to bring to the surface a portion of that asininity which lurks in the composition of the average man.

Sea-quarantine, whatever may be its inconvenience, seems to be, especially in the light of recent events, a success, and if it should prove only a partial one and cholera break through the barriers after all, it will be a success. Time gained, everything gained, is the parole in the present epidemic, when winter is near at hand.

Whether it is a wise plan to take hydrochloric acid as a prophylactic, should cholera make its appearance, is to my mind very questionable. Many persons do not bear it; it produces catarrh of the stomach in some, and aggravates existing ones in others, while in still others it has the well-known curative effect.

Should one drink the pure waters that are advertised as germ-free in case cholera should come to us? Yes, provided they are boiled, when they may prove as good as our Mississippi water after having gone that similar process.

It is a laudable and eminently proper undertaking that all over the country intelligent citizens form committees for the purpose of improving the sanitary condition of their cities. St. Louis has perhaps the best sanitary advantages of any of the large cities the world over. If these advantages are rightly comprehended and utilized the danger of a possible cholera invasion seems minimum. But there is a standing menace to the health and fair name of our city in case a serious epidemic of any kind should break out.

Time and again our city hospital has been branded, by the daily press, as a nuisance, and stigmatized as a burning shame on a rich and powerful commonwealth like ours, and I am afraid that, in case of an epidemic, whose danger is not by any means removed as yet, the scenes of horror witnessed in the hospitals of Hamburg would not only be duplicated but thrown in the shade. The condition, then, of that institution, on whose capacity and efficiency would above all depend the success or failure of barring and crushing out the invading enemy, an institution about whose inadequacy all the succeeding superintendents of the last twenty years have in vain complained, ought to

receive the attention of those who, in a spirit of magnanimity, have taken upon themselves the task Ne quid detrimenti capitat respublica.

The discouraging report of the Hamburg epidemic shows that, when once established, cholera generally braves all remedies, inoculation included. This should be an extra stimulus to work in the proper direction.