

# Henry Burden (1835–93)

President of the Ulster Medical Society

1888–89

## Presidential Opening Address<sup>1</sup>

Ulster Medical Society  
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GENTLEMEN, – I estimate too highly the privileges I enjoy on becoming the occupant of the post of honour to which your kind indulgence has elevated me, to be able to give adequate expression to my feelings. I must, therefore, content myself by simply asking you to accept my grateful, cordial, and sincere thanks for the confidence you have placed in me. I value my present position so greatly, because this Society has ever been the means of drawing into closer union the best blood of the profession in the North of Ireland, has at all times afforded a platform for the critical discussion of the latest phases in the evolution of medical science, and has created a source from which many practical results and sound doctrines have from time to time emanated.

Rochefoucauld has defined gratitude to be a lively sense of anticipation on the part of the recipient of a favour of the additional benefits he may count upon receiving from the donor in the future. I am free to confess that my gratitude partakes of this character, for I look forward with a keen foretaste of enjoyment to the benefits likely to accrue to me from a participation in your proceedings under such advantageous circumstances as those in which I am now placed. On casting about for a theme suitable to the present occasion I could light upon none that appeared more likely to prove interesting to you than a survey of the present aspect of bacteriology. I feel the more inclined to take up the subject, because, on a retrospective glance at the matters discussed by this Society during several years past, I find that no occasion has been exclusively devoted to its consideration, though several members have alluded to it in connection with other questions; and Dr. Workman, some two years ago, gave us the benefit of his valuable experience in respect of a portion of it. I purpose, then, to pass in brief review the more important of the recent additions to our knowledge of micro-organisms. Whatever may be the ultimate verdict of the profession with regard to the relations

they bear to disease, there can be no question that at the present moment they engross – and will probably for a long time to come continue to command – a very large share of attention, both on the part of the medical world and on that of the general public. The amount of solid work and concentrated thought that has been expended in the endeavour to solve problems in connection with them is without parallel in any single department of medicine. With few exceptions, the micro-organisms which occur as parasites on or in the human body are claimed by botanists to be members of the kingdom over which they preside. Granting this, we nevertheless find that they differ from the higher orders of plants in relying for their material wants chiefly upon organic matter, in being destitute of chlorophyll, and in evolving a large excess of carbonic acid while they consume a corresponding amount of oxygen; all of which attributes, be it observed, assimilate them to animals. They are referred to the group of thallophytes termed fungi, and are included in the following three subdivisions of the latter – namely, hyphomycetes or moulds, blastomycetes or yeasts, and schizo-mycetes or bacteria. I shall confine my remarks to the schizomycetes, employing, however, the more familiar though less precise synonym – bacteria.

Bacteria are unicellular organisms, composed of a peculiar variety of protoplasm, which Nencki has termed mycoprotein. The periphery of the cell is denser than the interior, and is said to be formed of a substance nearly related to cellulose. This investment resists greatly the action of both acids and alkalis. Bacteria multiply by fission and likewise by spores. The process of cell division sometimes proceeds with such amazing rapidity that, according to Colin, a single bacterium may produce, in twenty-four hours, 16,000,000 new individuals. Spores may fall into and remain for long periods in a state of dormant vitality, in which condition they are termed resting spores. When placed in circumstances favourable to their development, these resting spores become active again and grow into the characteristic form of their parents. A well-ascertained fact of great practical importance with regard to spores is that they are much less easily destroyed by high and low temperatures, or other germicidal influences, such as the action of the various antiseptics, than the mature forms. Thus, for example, while a temperature above 60° centigrade kills the majority of the adult forms,

<sup>1</sup> Note: A lecture by Dr Burden, given to the U.M.S. on 20th March 1889, was presented in the U.M.J. (vol 58 pp 114–116) as his Presidential Address. It was not.

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their spores may continue to live when the thermometer indicates a temperature far above the boiling point of water. The forms presented by bacteria are the round, the oval, the spiral, and the rod-like. Sometimes these are produced into long, jointed filaments, or give rise to colonies in which the individuals are held together by a jelly-like substance. In the case of some bacteria, the same individual has been observed to assume very different forms at successive stages of its life. Ray Lancaster, many years since, showed this to be the course of events in the life history of bacterium *rubescens*. It is also a fact familiar to microscopists that an infusion in which micro-organisms are growing may exhibit a preponderance of some particular form at one period while at a later stage the fluid swarms with a widely different form to the almost entire exclusion of that one first seen. These and similar phenomena have led many excellent authorities to the conclusion that a transmutation of one species into another is of common occurrence.

Büchner, indeed, affirms that he has succeeded in changing hay bacillus – a non-pathogenic species – into the bacillus of anthrax by cultivating the former in infusions of meat. Koch, however, in vain endeavoured to obtain the results arrived at by Büchner. The evidence in favour of a mutability of species is regarded by Cohn and Koch as falling far short of demonstration, and the numerous pure cultivations carried on daily in bacteriological laboratories tend to confirm the views on this question entertained by these trustworthy observers. A large majority of authorities now, therefore, assume permanence of species to be a well-founded doctrine; nevertheless, seeing that the life histories of comparatively few bacteria have been thoroughly worked out, it would be rash to dogmatise on the subject. The possibility that a ubiquitous species like hay bacillus may, under such readily-obtainable conditions as those supplied by Büchner, adopt in exchange for its harmless character the virulent properties of anthrax bacillus, renders it desirable to investigate the problem with the utmost rigour. Bacteria have been met with nearly everywhere when carefully searched for. River water, spring water, rain water; even, according to Klein, distilled water contains them. Any fragment of earth transferred from the surface of the soil to a sterilised culture medium soon produces an abundant crop of them. The air teems with them to such a degree that in the densely-inhabited quarters of towns the mere pouring of a sterilised nutritive fluid from one flask into another is sufficient to ensure their appearance

in the latter. The air on high mountains above the snow-line, or over the ocean far from land, is probably free from them. The surface of the healthy body is a resting-place for numerous bacteria. The larger bronchial tubes contain many, but Tyndall entertains the opinion that the smaller tubes and the air vesicles are free from them, because complementary air, driven from the lungs across the path of a beam of electric light in a dark room, is instantly detected by its non-luminous track.

From its commencement to its termination the alimentary canal harbours micro-organisms, all, without doubt, introduced into it from the outer world through the medium of solid food, drink, and otherwise. The conclusion that this is the source from which they are derived is confirmed by the researches of Letzerich, who found that the meconium of infants who have not yet breathed yields none, though a very short time after birth they can be detected in the intestinal contents. In the cavity of the mouth a great variety of forms have been observed. Miller describes twenty-five.

The assertion made by Lister several years ago, that no species are discoverable in the healthy urinary passages, has been substantiated by many others. A host of the most expert bacteriologists have been at great pains to ascertain whether or no the minute beings under consideration infest the normal tissues or blood of man. Ballance and Shattock recently instituted inquiries having the solution of this problem in view, and have decided that the evidence is strongly in favour of their nonexistence in those situations. Though the opponents to this decision are neither few, nor by any means despicable, yet they constitute a clear minority. An aid to the solution of this question, which is evidently one of vast importance, is furnished by the results of experiments in which septic bacteria, artificially introduced into sound tissues and blood, soon perished.

As in the case of other living beings, bacteria cannot continue the active exercise of their functions unless their environment supply certain essential conditions, such as moisture, appropriate food, and a temperature neither too low nor excessively high. They display, however, a remarkable aptitude for maintaining their vitality during long periods in a dormant or quiescent state, in the absence of either food or moisture, or both, and some can resist the adverse influence of an extremely low temperature. Anthrax bacillus has been known to survive a temperature of minus 140° centigrade.

Their food consists largely of proteinaceous matters, hence the nonpathogenic species find their

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most congenial soil in the dead bodies of animals and plants, or in the products of their decomposition, while the pathogenic forms flourish in the living tissues and fluids of their hosts. Most of them show a marked predilection for a special nutritive medium. Thus, the bacillus of tubercle is with difficulty cultivated outside of the living body in any other fluid than blood serum. An experiment of Naegeli shows how an apparently slight change in the nature of the soil may affect injuriously, or the reverse, the life of minute organisms. He found that in a neutral liquid, holding sugar in solution, and in which moulds, yeasts, and bacteria were present, the bacteria soon began to predominate, and give rise to lactic acid fermentation – on adding half per cent. of tartaric acid, yeasts prevailed; and when 4 to 5 per cent. of tartaric acid was mixed with the fluid, moulds got the upper hand. In the artificial cultivation of bacteria it makes a material difference whether the medium employed be acid or alkaline, even a slight excess of acid being detrimental to the growth of the greater number. Again, Koch found that while he could, by inoculation with certain bacteria, bring about septicaemia in the house-mouse, he was unable, by introducing the same organisms into the bodies of field-mice, to produce a similar effect; a result paralleled by the well-known difference in the susceptibility of different human individuals to the poison of specific diseases, supposed to owe their origin to micro-organisms.

Simple though they appear to be in form and structure, minute to the verge of visibility, even with the aid of the highest powers of the microscope, few of them endowed with the power of locomotion, yet to the vital actions of the infinite host of bacteria are now ascribed injurious and destructive effects upon the higher forms of organic matter, both living and dead, undreamt of by the most speculative philosophers until quite recent times. They are to-day believed to be the cause of all putrefactive processes, of fermentations, and some of the most damaging and deadly of the diseases that the human race is subject to. In discussing the relations that bacteria bear to disease, it has been found convenient to consider them under the following heads, namely – septic, zymogenic, and pathogenic bacteria.

Most of the septic bacteria are unable to establish themselves in living tissues or fluids, and when they are designedly placed in these situations by the pathological inquirer, they soon die. They usually occur only in connection with wounds and ulcers, or abscesses and gangrenous parts to which the air has access. Being the supposed efficient

agents in the production of putrefaction, and few localities being devoid of their presence, it is obvious that the lesions just named are momentarily liable to be invaded by them and become putrescent, unless they be protected by efficient antiseptic dressings, or kept free from dead and putrescible matter by drainage tubes and the strictest cleanliness. Septic bacteria are alleged to give origin to those poisonous alkaloids – the ptomaines, which are found in proteid substances undergoing putrefaction. The widely-distributed bacterium *termo*, familiar to all bacteriologists, may be quoted as an easily-obtainable and characteristic example of the septic group. Zymogenic bacteria are so called because they effect certain chemical changes in organic matter analogous to those that lead to the formation of alcohol. Articles of food and some of the secretions are the seats of their special activities, so that they are objects of interest more from a chemical than from a pathological point of view. A well-known example is the *micrococcus ureae*, which converts urea into carbonate of ammonium.

But the micro-organisms which have excited the deepest and most wide-spread attention are unquestionably the pathogenic bacteria. Pathogenic bacteria are intimately associated with specific diseases, in many cases standing, it is believed, to the latter in the relation of cause to effect. Koch, however, warns us that in no instance can it be said to have been satisfactorily proved that a particular infectious disease is due to a particular microorganism, if any of the following conditions remain unfulfilled; – (1) It is absolutely necessary that the micro-organism in question be present either in the blood or the diseased tissues of man, or of an animal suffering or dead from the disease. (2) It is necessary to take these micro-organisms from their nidus – from the blood or tissues, as the case may be, to cultivate them artificially in suitable media – i.e., outside the animal body, but by such methods as to exclude the accidental introduction into these media of other micro-organisms; to go on cultivating them from one cultivation to another for several successive generations, in order to obtain them free from every kind of matter derived from the animal body from which they have been taken in the first instance. (3) After having thus cultivated the micro-organisms for several successive generations, it is necessary to re-introduce them into the body of a healthy animal susceptible to the disease, and in this way to show that the animal becomes affected with the same disease as the one from which the organisms were originally derived. (4) And finally, it is necessary that

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in this so affected new animal the same micro-organism should again be found.

Through this trying ordeal many bacteria have passed, and turning up unscathed at the last stage of the process, have thus manifested at once their remarkable vitality, and the leading part they play in the causation of the diseases with which they are associated. But on attempting to submit some of them to these exacting tests, bacteriologists have encountered obstacles which, up to the present time, have proved insuperable. The bacillus of leprosy, for example, cannot be induced to grow and multiply in any medium yet provided for it outside the body of its host. Then again, every animal yet tried has refused to take the disease when inoculated with the bacillus of cholera.

Sufficient evidence is not forthcoming that the bacteria of infectious diseases ever penetrate the uninjured skin. There can, on the other hand, be little doubt that they gain access to the deeper parts by means of open wounds or abraded surfaces, and that they pass through the mouth and nose into the lungs or alimentary canal. Having once obtained admission into the body, a struggle for the ascendancy, probably in all cases, begins between them and the tissues. If the tissues be strong and healthy and the bacteria weak, so much the worse for the latter; but if the bacteria be vigorous and the vitality of the tissues depressed, then the bacteria become masters of the situation. They may now be arrested in their progress and manifest their presence by local lesions, or, having reached the blood-vessels or lymphatics, they may be conveyed by the circulation of those fluids to distant parts of the body. In the vessels they have been observed to cause coagulation of the blood. Fragments of the coagula so formed enclosing them in their meshes are liable to become detached and carried away by the blood-stream to smaller vessels or the capillaries, where, in the form of emboli, their career is cut short. The bacteria contained in these emboli become fresh centres of infection. The interior of leucocytes and the fixed protoplasmic corpuscles of the tissues appear to be an occasional *habitat* of bacteria. Whether the former engulf the latter in the same manner that the amoeba swallows its prey, or the micro-organisms are themselves active agents in their transfer to those situations is difficult to determine. Metchnikoff's observations may help to a solution of the question. In the frog he has been an eye-witness to the deglutition and apparent digestion of the anthrax bacillus by leucocytes, and certain cells of large size on which he has conferred the epithet phagocytes.

Do bacteria bring about the injurious effects attributed to them owing to the irritation produced by their mere presence, or by catalysis, or through the medium of a poison which they are supposed to elaborate, or by setting up a process analogous to fermentation? My answers must be brief.

Simple irritation seems insufficient to account for the phenomena. Catalysis, as commonly understood, is, in my opinion, a meaningless term. Fermentation does not appear to furnish a plausible explanation; but there are substantial grounds for the belief that certain poisons are generated by the vital actions of these micro-organisms, and that to them are chiefly due the pathological events that follow the introduction of the latter. These poisons have not yet been isolated; but it is worthy of note that in putrefaction bacteria are believed to be instrumental in the formation of the ptomaines – alkaloids producing symptoms of poisoning very similar to some of those observed in infectious diseases.

If the spread of infection be really due to the conveyance of specific organisms from one person to another, it is obvious that the organisms must, previously to their transference, have been eliminated from the bodies of the sick. Careful search has been made in the excretory organs and their excretions for micro-organisms. The bacillus of tubercle has been discovered in the expired air of phthisical patients. The intestinal evacuations of cholera and typhoid fever have yielded the bacilli peculiar to those diseases. An examination of kidneys removed from persons who have died of pyaemia, diphtheria, and scarlet fever has disclosed characteristic micrococci. The desquamated epithelial cells of scarlatina exhibit micrococci; but that these are specific cannot be positively affirmed. Through what variety of being micro-organisms pass during the intervals between their lodgments in the bodies of their successive hosts, unless their change of residence be more or less expeditious and direct, can scarcely be said to have been definitely ascertained as regards any.

The classification of bacteria is admittedly in an unsatisfactory condition, arising from the following circumstances; – (1) The close similarity in form, size, and structure of different species. (2) Their excessively minute size, which only permits of approximate measurements. (3) The probability that the same species may vary in size in consequence of differences in the nature of its environment. (4) The different forms assumed by some species at successive stages of development. (5) Our ignorance of their complete life-histories. On the other hand, it is true that we are aided in our discrimination of

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species by observing the manner in which chemical re-agents and stains act upon them, the characteristic figures that aggregations of them assume in culture media, and their pathological effects. Several elaborate classifications have been proposed, and more or less extensively adopted; but as none of them are likely to remain long in use, a simple classification founded on peculiarities in form, is, for the present at least, preferable.

I would therefore refer all pathological species of bacteria to the four following groups, viz.: – (1) Sphaero-bacteria, of which micrococcus is an example. (2) Micro-bacteria, with bacterium as its type. (3) Desmo-bacteria, claiming bacillus as a member. (4) Spiro-bacteria, including the characteristic genus, spirillum. Various other cross-divisions are occasionally employed for special purposes. Thus, Pasteur has divided bacteria into those that flourish only when exposed to the influence of the atmosphere and a group that thrives well in the absence of air. The former he terms aerobic, and the latter anaerobic. In a short *resumé*, such as the present sketch must necessarily be, it would be impossible to attempt even a passing allusion to every micro-organism that has been held accountable for disease. I shall then, in illustration of the foregoing general remarks, limit myself to a detailed account of three. The three I have selected are – the bacilli of anthrax, of tubercle, and of cholera. The first, because its life-history has been more fully elucidated than that of any other; the second on account of its paramount importance; and the third, seeing that a vast amount of attention and research has recently been devoted to it.

Bacillus anthracis is a species of the order desmo-bacteria. It inhabits the bodies of men and animals suffering from the disease variously termed anthrax, splenic fever, wool-sorters' disease, malignant pustule, charbon, Siberian plague – where it is met with chiefly in the blood, and more especially in the blood of the spleen. This organism exhibits a cylindrical or rod-like form, with slightly concave ends, and is of large size, measuring from 5 to 50 micrometres in length, while its short diameter averages 1 micrometre. It multiplies rapidly by division in the blood of its host, or when cultivated at a temperature of between 15° and 43° centigrade in suitable media. In the latter situation the rods produce in their interior highly-refracting, brilliant, oval bodies. These, which are the spores, measure about 1 micrometre in breadth, and 2 to 3 micrometres in length. They are not easily stained by ordinary dyes, but when treated with a hot solution of

fuchsin for twenty minutes they assume a red colour.

This bacillus needs air for its complete development, and comes therefore under Pasteur's aerobic division of micro-organisms. It is incapable of spontaneous movement. According to Klein, any fluid containing proteid matter is a suitable nutritive medium for it. During cultivation in such media the bacilli grow out into long, jointed and convoluted filaments, often twisted together like the strands of a rope. Freezing arrests the development of the rods, but does not deprive them of life. Drying and a temperature under the boiling point of water kills them. Spores, on the other hand, retain their vitality when dried, and resist a temperature of 100° centigrade for fifteen minutes when moist, but for an hour if dry. A very minute quantity of blood, taken from an animal ill of anthrax, when inoculated into a rodent, reproduces the disease in it; the animal usually dies in about forty-eight hours. Bacilli from its blood, after propagation through many generations, ultimately yield a pure cultivation. A susceptible animal, inoculated with this product, takes the disease, and in its blood bacilli can easily be detected. The majority of rodents and herbivora are very susceptible to infection. Rats, though rodents, are not readily infected; pigs, dogs, and cats are infected with the greatest difficulty. The bacilli have been, for the most part, observed in the blood, the capillaries of the spleen, lungs, kidneys, and indeed of nearly every organ in the body, being often packed full of them. The histological elements are seldom invaded. Malignant pustule is, however, at first a strictly local lesion, and if the diseased part be removed early the bacilli may never appear in the blood. These micro-organisms may enter the body through the medium of the lungs, the alimentary canal, or wounds and abrasions of the integument and mouth. Koch produced anthrax in sheep by feeding them with potatoes containing spores. Wool-sorters' disease arises from the inhalation of spores, detached from the fleeces of animals that have died of anthrax, by persons handling them. Malignant pustule – which has an origin similar to that of the last-named disease – attacks the exposed parts of the body, usually the hands and face, the bacillus probably reaching the subcutaneous tissue through some breach in the skin.

Bacilli are believed to be in some cases conveyed by flies, and on other occasions by the teeth of dogs that have eaten the flesh of the infected animals. Direct transference of bacillus anthracis from individual to individual rarely occurs, so that the parasite commonly leads a longer or shorter independent existence from the time that it leaves

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one host until it reaches the next. Now spores are not formed while it is in the living body, consequently when it becomes free it is liable to speedily perish by drying up or otherwise. If, however, it be at once exposed to the combined influence of the air, moisture, the organic matter of the soil, and a high temperature, it produces spores, and these can survive the vicissitudes of climate for more than a year. Summer heat returning, the spores germinate, and yield a new crop of bacilli. The blood, excretions, or carcase of an animal that has died of anthrax, may thus furnish a centre of infection in the pasture during a succession of years. Judging from Klein's observations in the case of mice and guinea-pigs, if the dead bodies of infected animals were, without delay, buried deeply in the soil, the bacilli would die without the formation of spores within a couple of weeks, owing to the absence of a free supply of air. Pasteur's assertion that spores are formed in the buried bodies of infected animals, and are brought to the surface by earth-worms, seems to have been disproved by the researches of Koch and others.

By cultivating anthrax bacilli under special conditions, Pasteur has succeeded in modifying their virulent properties in such a manner that, on inoculating them into cattle, the latter, after having suffered only slight injury from the operation, are rendered insusceptible of the disease for a year or more. The bacilli thus changed in character he terms attenuated virus. One of the processes by which Pasteur effects attenuation consists essentially in the cultivation of the bacilli in chicken broth freely exposed to the air, while the temperature is carefully kept at about 108° Fahrenheit. Chauveau brought about attenuation by heating bacilli to 52° centigrade for a quarter of an hour. Toussaint obtained a similar result by applying a temperature of 130° Fahrenheit for ten minutes. Chamberaud has succeeded in securing attenuation by the action of weak carbolic acid. Klein has directed attention to the noteworthy fact that anthrax bacilli, in passing through different species of animals, become endowed with different qualities. He writes:— "While, for instance, the blood bacillus of sheep or cattle dead of anthrax invariably produces death when inoculated into sheep or cattle, after passing through white mice it loses this virulence for sheep and cattle."

The bacillus of tubercle is one of the desmo-bacteria. It has been so uniformly detected in all varieties of tubercle when carefully sought for, that few pathologists now venture to deny that, if not the actual cause of, it is at least intimately associated with, the tubercular lesion. It presents the

appearance of a very minute rod, 2 to 5  $\mu$  in length by .3 to .8  $\mu$  in breadth. The extremities of the rod are convex. Stained specimens show clear spots, which were at first taken for spores, but the true nature of which have not yet been satisfactorily determined. Sometimes the rods bear a very close resemblance to a linear series of micrococci. Their cultivation exacts great care and special media, in which respects they differ remarkably from anthrax bacillus. Small portions of tubercle containing them, when placed on blood serum rendered solid by gelatine and sterilised, slowly develop, if the temperature do not vary much from 100° Fahrenheit, into plates or scales of a dull white colour. These scales are found, on microscopical examination, to be composed of bacilli, placed end to end so as to form curved lines. The most favourable temperature for cultivation is about 99.5° Fahrenheit, and development ceases when the thermometer falls to 82°, or rises to 108°. Tubercle bacilli are apparently, like those of anthrax, incapable of voluntary motion. A temperature of 212° Fahrenheit kills them in fifteen minutes if they be kept moist, but should they be dry they may retain their vitality for half an hour or an hour. They are destroyed by various germicides – as, for instance, a one per thousand solution of perchloride of mercury, and a five per cent. solution of carbolic acid. There is no proof that they enter the body through wounds or abrasions of the skin, but their introduction into the alimentary canal with food, and into the lungs in atomised fluids, has induced tubercle in the animals experimented upon. When they gain admission to the tissues of the body they spread, according to Baumgarten, through the agency of leucocytes, but in the opinion of others by means of the lymph spaces and vessels. Their relations to the giant cells of tubercle has been much canvassed. They have been supposed by their presence to cause the formation of these corpuscles. Now, no valid reason can be advanced why we should look upon the giant cell as a structural feature distinctive of tubercle, or assign to it a leading part among the morbid processes that take place in this lesion. Well-formed giant cells are met with in many tissues, both healthy and diseased – for instance, in the red marrow of fully-formed bone, in osseous tissue during its growth and also whilst undergoing removal either physiologically or pathologically, in the spleen, in myeloid sarcoma, in syphilitic gummata, and among the products of many non-specific inflammatory actions. Again, while in cattle, poultry, and horses bacilli are very numerous in giant cells, they are very rarely observed in that situation in the human subject. Payne says that he has

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never seen bacilli in the giant cells of human tubercle, and that other observers of large experience have confirmed this negative result. Meigert thinks that the bacilli penetrate the walls of veins, and thus reaching the blood-current, are carried to distant parts and cause general infection. Koch, in a case of acute tuberculosis, discovered them in the wall of an artery, and from that circumstance inferred that they may enter the arterial circulation, and thus become widely disseminated. Koch's classical experiments, undertaken with a view to the determination of the precise connection of tubercle with bacillus, though numerous and varied, may, in general terms, be described in a few words. He placed a minute fragment of tubercle containing the micro-organism on an appropriate soil and obtained an abundant crop. A few bacilli were removed from this cultivation to a fresh medium where they multiplied a thousand-fold. A small fraction of this growth was transferred to a new culture ground, and the process repeated again and again until the organisms were practically cleansed from every particle of the foreign matter that they originally carried with them. From the pure cultivation procured in this way a portion was taken and inoculated into the body of a healthy animal, in which, thereafter, the characteristic lesion appeared. Lastly, the tubercular matter in this animal, when subjected to microscopical examination, exhibited the bacillus. A host of competent observers have confirmed Koch's statements, so that there can be little question of their trustworthiness. Some species of animals suffer from the injurious effects of tubercle bacillus to a greater degree than others. In inoculation experiments, for instance, the greater number of rodents are easily infected, and ruminants, though less susceptible than rodents, are more so than dogs and cats. Different human individuals are clearly not equally susceptible, else few could escape infection. The following passage in Klein's work on micro-organisms is interesting from several points of view:— "According to my own experience, extending over a very large number of cases of human miliary tuberculosis and tuberculosis in cattle, I cannot for a moment accept the statement that the bacilli found in the two affections are identical; for I find that in the two diseases their morphological characters and distribution are very different."

Whereas anthrax bacillus is capable of leading an active non-parasitic existence, there is reason to believe that the bacillus of tubercle is a true parasite, its vitality outside the living body of an animal remaining in a dormant condition until a new victim is secured. Leaving out of view other considerations, we

need only recall to mind the difficulty with which its growth and multiplication are artificially induced to be convinced that the soil and climate of our own country at least do not supply either a nutritive medium suited to its wants, or that high and uniform temperature apparently so essential to its activity. Nevertheless, the bacilli in the dried condition retain their vitality in a potential state for a long time, even when subjected to great variations of temperature. Those expelled from the lungs in sputa or with the breath lose their germinative capacity after about six months.

The micro-organism formerly termed cholera bacillus, and regarded as a desmo-bacterium, is now by many authorities referred to the order spiro-bacteria, under the new title spirillum cholerae Asiaticae. The cholera reports of Strauss and the French Commission, and the German Commission with Koch at its head, are still fresh in our memories. It was in the sixth report that Koch announced his discovery of the cholera bacillus. Its form is that of a curved rod from .8 to 2  $\mu$  long, and from 1/3 to 1/6 of this measurement in thickness. The name comma bacillus, by which it is widely known, is evidently derived from its shape. When several are united end to end they form a spiral filament. They are endowed with the power of spontaneous motion, which is both rotatory and progressive. No internal spores have been clearly demonstrated. This micro-organism is without difficulty cultivated in a great variety of media – for instance, on gelatine, agar-agar, and potato; likewise in milk, broth, and blood serum. The media must be neutral or slightly alkaline; in an acid medium it will not grow. Its optimal temperature is from 84° to 104° Fahrenheit. When the temperature is reduced below 60° development ceases, though the organism still continues to live until the thermometric reading is considerably below the freezing point. Drying quickly kills this spirillum – a fact well worth bearing in mind. Long before the discovery of a specific organism the medical profession had with wonderful unanimity arrived at the conclusion that the materies morbi of cholera was conveyed to the alimentary canal of patients by means of drinking water, especially such as was contaminated by the entrance into it of the intestinal evacuations of persons already suffering from the disease. It was therefore with feelings of considerable satisfaction that they learned from Koch his discovery of comma bacillus in a water tank at Calcutta, in the neighbourhood of which cholera was known to exist. On the other hand, Klein, Gibbes, and Cunningham have met with comma bacillus in tanks and on water

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plants where there was no reason to suspect that it had anything to do with the causation of the malady. In connection with this question an important fact has been ascertained by experiment – namely, that the bacillus may remain in spring water for seven months and still be capable of development if placed in a congenial soil. Even in distilled water it may retain its vitality for at least ten weeks. Having gained admittance into the alimentary canal, the bacillus appears, in most cases, to be confined to that region, rarely penetrating the wall of the intestine. It has seldom been detected in the blood or tissues, and when artificially introduced into the blood it speedily disappears. Organisms so similar to the comma bacillus in form as to be indistinguishable from it by the microscope have been seen in cholera nostras, in the intestine of guinea-pigs, in the mouth, and in dejecta from the bowels of persons in good health. But the peculiar form and mode of growth of the cholera bacillus in culture media is said to distinguish it from all others. Granting this, it has never been met with in any other disease than Asiatic cholera, in consequence of which circumstance it is looked upon as a diagnostic indication. Although its existence and its presence in cholera are admitted by nearly all qualified observers, yet much difference of opinion prevails as to its relation to that affection, Koch and Virchow holding it to be the cause of the latter, while Klein and many others believe that this position is, in the present state of our knowledge, untenable. A very significant gap in the chain of evidence is the fact that no animal yet experimented upon, with the doubtful exception of the guinea-pig, exhibits symptoms which bear even a remote resemblance to cholera. The dejecta from cholera patients have been administered with their food to pigs, dogs, cats, and monkeys, yet the effects have not been such as to justify the opinion that they were cholera-stricken. Subcutaneous injection of the bacilli from various sources proved equally inefficient. In guinea-pigs alone have symptoms been observed which, taking into account the, in many respects, vast difference between their organisation and that of man, might be regarded as choleraic. Comma bacillus probably produces its evil effects by elaborating a poison which is absorbed through the intestinal walls.

And now it is full time that I brought my discourse to a close. In doing so I would remark that though what I have said may possibly seem slight and sketchy, nevertheless it is the result of much sifting of a considerable amount of conflicting evidence. I have, in fact, as Huxley puts it, endeavoured to play the part of a sieve, and to separate the well-established and

essential from the doubtful and unimportant portions of the subject. In bacteriology, “there is,” in Foster’s words, with reference to another science, “a zone of strife where truth and error mingle in conflict, and where the results of yesterday have power because they are new. This agonosphere is merely the envelope of a solid nucleus of acquired truth which, year by year, grows larger at the expense of its more fluid and gaseous wrappings.”

It has been my aim throughout this address to keep, as far as possible, clear of the zone of contention.