LECTURES

ON
THE OCCURRENCE OF ORGANIC FORMS
IN CONNECTION WITH CONTAGIOUS
AND INFECTIVE DISEASES.*Delivered at Owens College, Manchester.*

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LECTURE I.

THE subject of the present lecture is the relation of bacteria to the chemical and physical processes which constitute the life of the higher animals.

One of the first questions which suggests itself to the mind in approaching the subject is this: How does it happen that these bacteria, which we suppose must have existed half-a-dozen years ago in as great numbers as at present, were then scarcely heard of, and that they now occupy so large a place in the medical literature of this country and of Germany, and have lately afforded material for lively discussion in the French Academy? To us in England the subject is chiefly associated with the truly scientific investigations of Lister—the first to show its practical bearing on the pathology of traumatic diseases. In Germany, there can be no doubt that the extensive inquiry which is now being carried on by so many persons, took its start from the laborious researches of a poor professor of botany at Jena, who, with defective resources, bad instruments, and in spite of discouragement and disparagement of all kinds, has persisted for many years in his strivings to work out this intricate question. Unfortunately, he lost his way at an early stage of his enterprise, and, like many pioneers in exploration, has accumulated results of which it must be admitted that the value is scarcely proportional to the quantity. Need we be surprised that, of the many who are quite ready to sneer at Hallier and his cholera-fungus, few, if any, have undergone the labour of reading his papers?

As introductory to my subject, I must first give a short account of the natural history of the organic forms which we now, following high botanical authority, group together under the term bacteria. Secondly, I shall consider the question of their general influence on the processes of life of the higher animals, and the mode in which this is exercised. This will prepare us for discussing the question how far they act as morbid poisons, or as the vehicles of such poisons, or are characteristic of specific diseases. I would remind you that the question we have before us is not that of the origin of bacteria, nor that of their place in nature, but the more restricted one of their influence on ourselves, and on the lower animals whose life, whose health, and whose diseases are but the counterparts of our own.

It is because they are constantly invading our bodies and attacking the living protoplasm by which the work of life is carried on in our tissues, that we, as pathologists, take an interest in their natural history. It is for this reason that questions relating to them, which at first sight seem remote and remote, have a direct and immediate bearing on practical questions. For if, as I shall endeavour to show, they are constantly present to us—constantly mixing up their life with ours—we cannot wisely remain ignorant of their nature. We do not aspire or profess to be botanists; but, if plant-forms and plant-life associate themselves with the very processes which it is our business to study, we must become botanists for the occasion.

In the short introductory account I shall give of the forms of bacteria, I shall follow Professor Cohn (*Ueber Bacterien, die kleinsten lebenden Wesen*, Berlin, 1872), as being the only botanist of high authority who has given special attention to the subject. For the remainder of what I intend to say, I am myself answerable. I shall, however, make it my endeavour not to vindicate the views which I have advanced myself, or which others may have attributed to me; but to place before you a general view of the work that has been done during the four years which have elapsed since the subject began to occupy the serious attention of pathologists.

MORPHOLOGY AND NATURAL HISTORY OF BACTERIA.

The first fact that I shall advance with respect to bacteria is, that they are the smallest and least organised of all living beings. As regards size, it is best to judge by comparison with objects with which we are microscopically familiar. The most common rod-like forms are

in length about one-third of the width of a blood-corpuscle; *i.e.*, about $\frac{1}{1000}$ th of an inch—so small that, if we examine a liquid containing them, with the ordinary magnifying powers used for histological observations, we can scarcely be said to see them to any practical purpose. It is necessary to have recourse to the best microscopes and the highest powers, if it be desired to observe them in such a way as to arrive at useful results.

What grounds have we for stating that they are the lowest organisms? One is, that they present only very slight differentiation of parts; but in this sense they are certainly not simpler than many other forms that might be referred to. The chief ground for the statement lies in this, that they are much less *specific* in their characters—much more under the influence of the conditions under which they originate and are developed—than organisms of any other class. Just as in the higher animals and in man himself we call those functions lowest which are most completely automatic—*i.e.*, most completely under the guidance of known conditions—so also, as regards form, we recognise that while all animal and vegetable forms, even the highest, are moulded by circumstances to fit their places in the economy of nature, this moulding power—this adaptation of form to circumstance—becomes more and more obvious the lower we descend in the scale of development.

The next fact relates to the *habitat* of bacteria—to the medium in which they live—water. They inhabit water either as such in the ordinary sense, or in the various conditions recognised as *moisture*, whether occurring on damp surfaces or as filling the interstices of solid bodies, which bodies, when so impregnated with water, are said to be damp. Those who are familiar with chemical work, know that this quality of dampness goes a great deal further than the popular notion of it; that many things ordinarily called dry, yield, when subjected to the drying processes commonly used in the laboratory, evidences of being really moist. Consequently, moisture, regarded as a limiting condition of bacterial life, is a very wide and comprehensive one.

From this statement, it must not be understood that bacteria do not exist in the atmosphere. But their existence there in an active form strictly depends on moisture. They attach themselves, without doubt, to those minute particles which, scarcely visible in ordinary light, appear as motes in the sunbeam, or in the beam of the electric lamp. It is by the agency of these particles that they are conveyed from place to place.

Notwithstanding that the word bacterium means a rod, and that many of the forms to be immediately referred to are not rod-like, I am obliged to use it, because it is used by others as a general term for the whole group of organisms known to botanists as *Schizomycetes*. This designation being obviously too long, I attempted, in 1870, to introduce the word *microzymes*, a word which was intended to denote the fact that, in the development of these organisms, the process of vegetation is always associated with chemical processes of a peculiar kind, in a way comparable to that in which the vegetation of the yeast-plant is associated with the alcoholic fermentation. I forego the use of the word microzyme for the reason I have mentioned, *viz.*, that it has not been taken to, but I am not the less sensible that such a word is as much needed now as ever; for it is evidently inconvenient to say, as I now find myself compelled to say, that bacteria—rods—may be either globular, egg-shaped, or filamentous. Cohn classifies our organisms under terms expressive of these various forms, the most important being micrococcus, bacterium, vibrio, and spirillum. I have drawn these on the black board.

Bacteria have, as a rule, two states of existence—a state of activity and a state of rest. When a liquid teeming with bacteria in the active state is observed under the microscope, the attention is so riveted, that it is an effort to take away the eye from the instrument. The movements have been often described. In the case of rod-shaped bacteria, the axial movement in which the rod advances or retreats in the line of its axis, the direction being frequently reversed, is the most common. This kind of locomotion occurs often by fits and starts, the body remaining in the intervals quite still, or assuming a pirouetting or spinning movement. In all rod-like bacteria, it is probable that the progressive or axial movement is associated with rotation, for, in observing the motion of vibrios, it is easy to see that they, in progressing, twist round the axis of the spiral. When this is the case, it looks as if the filament were executing a wriggling motion, *i.e.*, as if its body were contractile; but this is obviously deceptive. The mechanism of the motion is as little understood as those of *Oscillatoria*, which it closely resembles. It must be carefully distinguished from the passive motions which are exhibited by all particles of size comparable to that of bacteria, when suspended in a liquid of which the density does not differ very widely from their own. We shall find afterwards that certain forms of bacteria appear to be motionless in all stages of their existence.

Rod-bacteria multiply by repeated bisection. This mode of multiplication goes on continuously, the rate varying with the conditions of life, and particularly with temperature. Under favourable circumstances, it is enormous. From actual measurement of the time which elapses in a single case between a bisection and the division of each half into quarters (in other words, of the longest time that a single bacterium remains without dividing), it has been ascertained that the interval in question, in common bacteria is about an hour. This being the case, it is easy to compute that every single bacterium must produce 16,777,220 individuals in twenty-four hours. Putting it otherwise, the progeny of a mass of bacteria weighing $\frac{1}{2400}$ grain would, at the end of a day, weigh a pound.

In the largest forms of bacteria, it can be made out that each individual consists, not, like an animal cell, of one sort of living substance,* but, like a plant-cell, of a protoplasmic interior enclosed in an envelope of cellulose, by virtue of which the bodies of bacteria are enabled to resist the action of reagents, particularly weak acids and alkalies, which dissolve protoplasm. In those bacteria which separate from each other as soon as they assume the form of distinct individuals, the more stable external part presents itself as a mere envelope; but when, as very usually happens, the progeny which results from a continuous succession of divisions remains in a state of aggregation, the envelope appears to become identified with the "gelatinous" matrix by which they are held together. This observation was made more than twenty years ago by Cohn, who devised the term *zoogloea* as a general designation for the clumps, or, as Hallier calls them from the mode of aggregation above described, "colonies". You will find that this term is now very constantly used by writers on the subject, for these gelatinous masses occur under a great variety of circumstances. In form, they are mostly either spheroidal or membranous, and have this one characteristic which is noteworthy, that their structure is such as to indicate that they grow at their surfaces or margins, not interstitially. Thus, for example, in the spheroidal forms, which, as seen under the microscope, present a more or less circular outline, it is obvious that the multiplication of individuals is most active near the edge. The membranous forms, on the other hand, often present a growing outline in one direction, a disintegrating one in the other.

We are not able to state that the process of repeated division into two is the only one by which bacteria come into existence. When we watch a liquid in which they are beginning to appear as if spontaneously, where none were visible a few minutes before, all that we can make out is, that a nebula presents itself; and that here and there, in the previously homogeneous liquid, particles exist which, although their form is at first indistinguishable, eventually become recognisable as bacteria. As to the way in which this happens, it is difficult to speak positively, for with reference to it no evidence is admissible excepting such as is founded on direct observation—i. e., on watching the process in a single instance for many hours—fixing the eye on a single bacterium, a thing weighing two-billionths of a grain, and measuring one-eighth-thousandth of an inch, and not quitting it till it divides and divides again. Klebs has attempted to do this, but I will not detain you with an account of his researches.

From what I have said as to their structure and ordinary mode of multiplication by division, it is obvious that bacteria resemble plants, and particularly the *Oscillatoria*, more than animals. The proof that they are plants rests on what is known as the nature of the chemical processes which constitute their life, to the consideration of which we must now pass.

How do bacteria act on the medium in which they live? On this subject, we owe the foundations of our knowledge to Pasteur. The first fact is, that bacteria act on the media in which they live, not as animals, but as plants. Like plants, they derive the nitrogen that they use to build up new albuminous compounds, not from previously existing albuminous compounds, but from ammonia. Like other colourless plants, they derive their carbon apparently from any carbon-compound except carbonic acid, by dissociation of its elements. Like plants, they require certain inorganic constituents to be present in their soil, particularly potash and phosphoric acid.

As regards the assimilation (or fixation) of carbon, Cohn's researches have very materially advanced our knowledge since the publication of Pasteur's work. It was obvious that bacteria did not decompose carbonic acid under the influence of sunlight, by the same wonderful process by which that dissociation is performed by green plants. This they could not do in the absence of chlorophyll. But in this respect they were not

in any different position from the fungi, or even from the colourless phanerogamic parasites—as, for example, the bird's-nest orchis.

Pasteur's investigations* related, not to bacteria or to the organic forms which are associated with the process of putrefaction, but to the yeast-plant. With reference to that organism, he proved that it derives its nitrogen directly from ammonia. He proved at the same time that the cellulose of which the external part of the yeast-cell consists, is derived from grape-sugar, and cannot be formed in the absence of that body. He did not extend the application of these facts to the organisms of putrefaction; but it came to be assumed that what was true of the yeast-plant would also be true of the others—viz., that, although ammonia was a sufficient source of nitrogen, some hydrocarbon must be present to yield carbon.

Cohn showed this assumption to be a mistaken one, by applying to the organisms of putrefying liquids the same mode of investigation that Pasteur had before applied to the yeast-plant (Cohn, *Beiträge zur Biologie der Pflanzen*, Heft ii, pp. 191-202). That method (since known as the method of cultivation) consists in first finding a liquid of known chemical composition in which the plant to be investigated grows vigorously, and then gradually modifying the composition of this liquid by the elimination of one after another of its ingredients, until at last a mixture is obtained in which the greatest possible simplicity is combined with the greatest possible adaptedness as a soil to the requirements of the particular organism; adaptedness being judged of by rapidity of growth. Such a liquid, as regards the yeast-plant, is that known as Pasteur's cultivating fluid. Its composition stands for the fact that sugar and certain crystalline salts are all that is wanted for the nutrition of the yeast-plant.

In the earlier experiments as to the cultivation of bacteria, e.g., in those which I made in 1871, it was assumed that Pasteur's liquid would also be the most suitable liquid for bacteria. During the same year, however, Cohn, observing that, although bacteria flourished in it abundantly, it was very difficult to prevent the growth at the same time of the yeast-fungus and of penicillium, i.e., common mould, left out the sugar, and found that the bacteria flourished better without it than with it. His next step was to substitute for the solution yeast-ash (a material which is troublesome to prepare) a solution containing the required salts in about the proportion in which they are ascertained to exist in the ash of the yeast-plant. The liquid which we now use as a "cultivation liquid" for bacteria is prepared by dissolving half a percentage each of potassic phosphate and magnesian sulphate in water having a trace of calcic phosphate in suspension,† and then adding as required a further percentage of ammoniac tartrate, and of course boiling the mixture. In this liquid, bacteria grow rapidly—a fact which proves not only that they are able to take their nitrogen from ammonia, but that they can also derive carbon from the tartrate—the only carbon-containing body which is present. Although, however, it supports the life of bacteria so completely, that they not only subsist in it, but multiply with enormous rapidity under favourable conditions of temperature, it never originates them, if it have been boiled. It can, indeed, be very easily kept for indefinite periods without change, remaining absolutely transparent and barren, provided that care be taken to protect it from contamination. It is, however, much better practically to keep the solution of inorganic salts, adding the tartrate in the proper proportion for each set of experiments.

In order to determine the development of bacteria in a liquid of this kind, all that is necessary is to touch it with a "damp" surface—a glass rod, a thread of cotton or silk—any object which, having been exposed to the atmosphere, has not since its exposure been dried by heating it to a sufficient temperature. The result may be equally well attained by allowing a particle of dust or a drop of water, or common distilled water, to fall into the liquid. All these liquids, although they contain no organic forms which can be recognised even with the aid of the highest powers, yet contain that which, when added to solution of ammoniac tartrate, determines its decomposition, and the building up of its nitrogen and carbon into higher combinations—in a word, vegetation. I call this process quasi-spontaneous. It is not spontaneous, for this simple reason—that it is dependent on conditions which are so far known, that it is possible to control them with perfect certainty.

I may add, that it was by experiments such as those to which I have just been referring that I was enabled to show, in 1871, that moist surfaces and particles of solid material in suspension in the air play the chief part in the propagation of bacteria; i.e., in the conveyance of the material out of which they spring from one soil to another. This in-

* In using the expression, "one sort of living substance", I must guard against being supposed to mean that any kind of living protoplasm is homogeneous. Hyaline though it may appear, we are not able at present to assign any limit to its complexity of structure.

* The experiments in question are to be found in Pasteur's well known papers on Alcoholic Fermentation (*Annales de Chimie et de Physique*, tome lviij, 1858).

† The calcic phosphate is best prepared by precipitating solution of calcic chloride with common sodic phosphate, taking care that the former shall be in excess. This precipitate splits on boiling into a soluble and an insoluble phosphate.

ference has now been confirmed—I think I may venture to say, established—by very numerous observations.*

INFLUENCE OF BACTERIAL VEGETATION ON THE PROCESS OF PUTREFACTION.

In referring to Cohn's classification of the organisms which constitute the group of Schizomycetes according to their form, I stated that this classification was chiefly of value for the purposes of description, and that the exact similarity of any two forms cannot here be taken as evidence of their organic continuity any more than their dissimilarity affords indication of the absence of intimate relation between them; for the influence of environment over organisms such as bacteria is so great, that it seems as if it were paramount; the surrounding conditions claiming a power not merely of moulding the organism into conformity with themselves, but even of originating it.

For reasons on which it is unnecessary to enter here, we do not admit the latter part of this claim; but it is a principle of fundamental importance in dealing with the question we have now before us—that of the agency of bacteria in septic processes—that the influence of circumstance over form is practically so powerful, that, in considering the relation of bacteria to septic processes, we shall do best if we regard the appearance of particular forms as mere links in the chain of events of which the process consists.

To illustrate this, it will not be waste of time to refer for a moment to the singular fact discovered a short time ago by Professor Cohn, that, under conditions as yet quite unknown, colouring matters come into existence in albuminous liquids when left to themselves at ordinary temperatures; and that this development of pigment is associated with the development of bacteria. Not long ago, having left a "solution" of ordinary egg-albumen in a cupboard in the laboratory, I found that the liquid, which had no putrid odour, possessed an intense indigo blue colour. Being acquainted with Cohn's observations, I at once guessed what had happened, and found, on microscopical examination, that the blue scum on the surface of the liquid consisted, first, of colourless bacteria, resembling in form those met with in septic liquids; and, secondly, of blue pigment-particles of extreme minuteness, which appeared to be imbedded in the interstitial gelatinous material by which the organisms were surrounded. The process continued for some time; but eventually the liquid was inadvertently allowed to dry. On inoculating a similar albuminous liquid with the dried residue, I was unsuccessful in reproducing the process; but Cohn, who came upon several of his colour-producing bacteria in a similarly accidental way, was able to perpetuate the process by repeated transmissions.†

I mention this observation merely to illustrate what I have been saying as to the relation between the two collateral processes—between the vegetation-process, on the one hand, and that of the formation of a characteristic chemical product, on the other. Here we have no sufficient reason for saying either that the production of colour is the cause of the development of bacteria, or that the bacteria are the agents in the production of the pigment. All that we observe is, that the two phenomena begin, continue, and end together; we regard them, therefore, as collateral characteristics of one and the same process.

As the result of innumerable observations, we know that, as a rule, those changes in albuminous liquids, which we familiarly recognise as constituting putrefaction, are accompanied by the presence in such liquids of characteristic vegetable organisms. We also know that the two processes—viz., the chemical changes and the rapid vegetation go on *pari passu*, and that the same circumstances which favour the growth and multiplication of organic forms also favour putrefaction.

As to the meaning of these facts, there is some difference of opinion even among competent naturalists. All are agreed that the relation between the chemical process and the vegetative process is an intimate one; but somewhat discrepant views prevail as to its nature.

The fundamental experiment by which the intimacy of the association is proved is this. When a tube or flask is partly filled with water containing albuminous matter in solution or suspension, and subsequently boiled for a sufficient length of time, and closed hermetically during ebullition, no putrefaction occurs under any circumstances; but if, after such a tube has been heated and allowed to cool, a drop of distilled water, or any other exposed liquid, be added before the tube is again sealed, putrefaction follows, provided that the preparation is kept at the ordinary temperature.

As I have already hinted, there are some naturalists who would not agree to the terms in which I have stated this result. They would rather substitute for the words "under any circumstances" some such expression as "in 9,999 cases out of 10,000". For our present pur-

pose, it makes little difference whether the statement be accepted absolutely or not. But there is another point relating to the origin of bacteria in albuminous liquids of much greater importance, which the discussion about abiogenesis is apt to conceal, or throw unduly into the background. It is a question which arises directly out of the results of the "cultivation" experiments to which I have just referred. These experiments show that bacteria are able to derive the whole of the carbon they require for the building up of their protoplasm from compounds of great chemical simplicity, which have never formed part of any living organism, and seek for no higher source of nitrogen than ammonia. This being the case, it is more than probable that, when the growth of bacteria goes on in association with septic processes, they derive their nitrogen and carbon, not from the albuminous compounds themselves, but from the ultimate products of their disintegration. This being the case, we must regard bacterial life (in so far as it consists in the building up of new protoplasm) as a process consequent on the chemical process of putrefaction with which it is associated. For disintegration must already have proceeded as far as to the production of ammonia—in a word, must have proceeded to the last stage—before the new integration could commence.

While admitting this, it is important clearly to see that the admission does not in any way render it more or less probable that bacteria are the efficient causes of putrefaction—that without which putrefaction could not take place—for there is nothing which forbids us to regard bacterial vegetation as connected (if I may so express myself) with both ends of the chemical process of disintegration of putrescible material at the same time; not the shadow of an objection to the assumption that, on the one hand, bacteria derive material for the integration of their protoplasm from the products of *disintegration* of the soil in which they flourish, and, on the other, that they produce the ferment by which *disintegration* is determined. There is nothing, in short, against their standing to the chemical process at the same time in the relation of antecedent and consequent.

If it should seem to you that this is a too vague way of dealing with the subject, I would ask you to consider that the question is one in respect of which caution is more than usually necessary; for, while theoretical explanations offer themselves freely on every side, experimental investigation is beset with peculiar difficulties. As regards the main question, that of the agency of bacteria in producing putrefaction, there are two extreme views, which are both clearly mistaken—the one which asserts that they have nothing to do with the septic process; the other, that the chemical phenomena of putrefaction are the mere accidents of a peculiar kind of vegetation. The truth lies without doubt between these two opposed theories; but it is not to be got at by an ingenious reconciliation of the one with the other, but by honestly opening the mind to the facts as they stand, in the confidence that, if they are allowed fair play, they will eventually shape themselves into a general conception, in accordance with their true relation. So long as uncertainty exists, there is nothing to be so much avoided as that sort of clearness which consists in concealing difficulties and overlooking ambiguities.

[Since this lecture was delivered, an important contribution to the elucidation of this question has been made by Dr. Hiller of Berlin ("Der Antheil der Bacterien am Fäulnisprozess," *Centralblatt*, No. 54, Nov. 14th, 1874). Starting from the fact observed by himself (to the accuracy of which I can testify from my own observation) that, in the "alkaline fermentation" of urine, the splitting of urea into ammoniac carbonate is not in relation with the abundant development of septic bacteria in the liquid, he made experiments which showed that in urine, bacteria do not derive their nitrogen from urea, but from other sources; and that, if ammoniac tartrate be added to urine, the multiplication of bacteria goes on with great activity without any diminution of its acid reaction, *i.e.*, without any decomposition of its urea. From this result, he proceeds to similar experiments as to the influence of bacteria on egg-albumen. Having first ascertained, by careful observations, the fact familiar to the housewife that fresh eggs "turn" when put into the same basket with rotten ones, and can therefore be infected through the air, he injects a "cultivation liquid", containing bacteria, but not putrid, into the albumen of a fresh egg, with the aid of a subcutaneous syringe. The egg remains unaltered. He therefore thinks it impossible to identify multiplying bacteria with the "septic ferment"; with reference to which he thinks that the experimental investigations of the last few years have proved nothing more than "it is a particulate substance which either exists suspended in the air, or adheres to objects, and that it can be separated from the air by filtration, and can be destroyed by the temperature of ebullition". With this final statement of the case I perfectly agree, and am not at all disposed to quarrel with him because he goes on to suggest that the "particles" of which the septic ferment consists are not living beings, but *Proteinsplitterchen*.]

* On this subject, see Cohn, *loc. cit.*, p. 194; Landau, *Arch. für Chirurgie*, xvii, p. 531.

† Cohn, *loc. cit.*, p. 180.