LECTURES

ON

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

BY

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LECTURE III.

SPECIFIC CONTAGIA.

In the last lecture, we entered on the consideration of the question, whether or not, in those cases in which fever is produced by a poison of septic origin, the organisms which associate their life and development with all putrefactive processes, are concerned in the pathological phenomena which manifest themselves. It was shown, on the ground of experiment, that, although pyrogenic liquids in the crude state are septic, and, therefore, contain bacteria in greater or less numbers, it is possible to obtain from them a material of great activity, *leaving behind the microphytes*. In stating this fact, I pointed out that it would afford no ground for denying the influence of bacteria in the production of the morbid material; for, although they may not themselves constitute it, there is nothing in the fact observed which makes it less probable than before that they are concerned in those chemical changes of which its presence is one characteristic. At the close of the lecture, I drew special attention to a fact of great moment, namely, that, in my pellucid pyrogenic liquid, the active principle, although apparently in solution, is really particulate, for it can be separated by an appropriate mode of filtration (filtration through a "porous cell").

To-day we pass to a subject which must be kept apart from the other—that of the relation of microphytes to specific infections. The two questions are distinct by nature, and consequently the modes which have to be employed in their investigation are necessarily different. It is, therefore, desirable to keep them separate. In fever, we have to do with a process—an aggregate of functional disorders, all of which have their seat in the organism. In contagion, we have to account for its effect on ourselves, and also (what is more difficult) for its behaviour outside of us—the wonderful fact that it preserves itself for long periods, and is conveyed to immense distances quite independently of its ultimate destiny.

The doctrine that microphytes have to do with the process of contagion is based on two sorts of observations, viz., those relating to the physical characters of contagious liquids, and those relating to the existence of organisms of characteristic form in them. As regards the physical characters of contagious liquids, the fundamental fact is that contagium is *particulate*. I do not hesitate to use this word, for there is no other which answers the purpose. It stands for the general result of observations made by Chauveau as to the non-diffusibility of the infecting part of a great many contagious liquids, particularly those of small-pox, vaccine, glanders, the so-called small-pox of sheep, or sheep-pox. The method employed by Chauveau in these investigations is now so well known that I need only advert to it very shortly. As a link in the chain of evidence on which the notions we now entertain as to contagium are supported, it is too important to be omitted. The method, like that of which in last lecture we considered the application to the investigation of the fever poison, is one of mechanical analysis. A liquid known to be actively virulent is placed at the bottom of a small test-tube, which stands upright on a foot, or is otherwise supported in the same position, care being taken to avoid the slightest contact between the liquid and the sides. Water is then allowed to flow over the surface of the liquid until it forms a layer a few lines in thickness. The result is that, if the liquid remain absolutely still, diffusion takes place between the liquid and the water. The soluble salts pass into the water, along with a quantity of albumin: everything which is particulate remains below, everything that is diffusible rises. The process differs from that of diffusion through a membrane in this respect, that, whereas in the "diffusion cell" bodies which are very slightly diffusible, such, e.g., as albumin, pass through the membrane in extremely small quantity, so

that practically they may be said to remain behind, in the present case, the only constituent which remains at the bottom consists of particles which, although they are small enough to pass readily through filtering paper and act so little on light that they do not render the liquid turbid, can yet be seen under the higher powers of the microscope. Hence, if the contagium is particulate, it will be found exclusively in the lower layer; if diffusible, it will be in the surface layer of water, albumin, and salts. Experiment showed, as regards all the contagia I have mentioned, that it remained below; and, therefore, was insoluble and indiffusible.

These experiments were made in 1868-9. I became acquainted with them when spending some time at Lyons in the latter year, and afterwards repeated them in London in their application to vaccine. I had previously (in 1866) made analogous experiments on the contagious liquid of Rinderpest, but by another and very inferior method. I had introduced a liquid of known contagiousness into an ordinary diffusion cell, and had observed that the active part did not pass through the parchment-paper septum. This is a bad method, because in this kind of diffusion the albuminous compounds which are very slightly diffusible, are stopped by the septum; so that it might be objected that the toxic agent was contained in the albumin, not in the particles. Indeed, a blunder of this sort has been very recently promulgated by a French writer, M. Onimus.*

On this inference as to the particulate nature of contagium, I founded in 1870, an *a priori* argument in favour of the probability of *contagium animatum*—that is to say, in favour of the doctrine that the property of contagiousness as manifested in contagious morbid products is associated with the presence in such products of particles *which possess a life which is not that of the tissues of the human or animal subject of disease*. If contagium be conveyed from place to place and maintain its activity in the form of particles, those particles must consist either of bits of protoplasm or of living organisms; for those are the only sorts of particles of which we have any indication in contagious liquids.

Now, considering that of all perishable things protoplasm is among the most perishable—so much so, that no living particle of our bodies can be abstracted from its place in the organism, even for five minutes, without dying and being disintegrated—it appeared to me quite out of the question to suppose, as Dr. Beale had suggested, that the particles could be of this nature, consistently with the astonishing power which they evidently possess of retaining their activity for such long periods, in spite of their being subjected to enormous varieties of moisture, temperature, and all other conditions. And considering that life—i.e., organisation—is the only condition whereby a body of chemically unstable composition is enabled to hold its own against such disintegrating agencies, I thought then, and I still think, that the only possible explanation of this fact of the persistence of contagium was to suppose its particles to be living. Then at once the question arose—"What sort of life is it that they possess?" Two facts help us to conclude in favour of the group of organisms I described in last lecture; first, they are the smallest and simplest of known organic forms; and, secondly, they possess the wonderful property of passing into a state of persistent inactivity or latent vitality, in which they perform no function, but can be at any moment awakened up into active function whenever they are brought under favourable circumstances. If I am asked what ground I have for the statement, that bacteroid microphytes possess the property of latent persistence, I will content myself with drawing your attention to the undisputed facts relating to the inoculation of "test-liquids". If I find that a particle of dust which has remained on the ceiling of the room for some time, when added to a solution of ammoniac tartrate, determines an enormously active vegetation of bacteria in it, I find it difficult not to suppose that the particle of dust contains living material; and inasmuch as I know that, if I examined it under the highest powers, I should see nothing which I could recognise as vegetable by any vital manifestations which it would present to me, I am compelled to express the result of the experiment in some such terms as I have used. Particles are there, which, so long as the dust remains on the ceiling, undergo no changes, manifest no process. You may object that I have no proof that the dust contains anything living. True; but I have proof that it contains that which produces life, and express this state of things; viz., the absence of manifestations of life, on the one hand, and, on the other, the fact, that the stuff in question possesses the power of impregnating something else which before was barren, by saying that the dust possesses latent vitality.

I have now to run over, as briefly as possible, the cases in which observations have been made as to the presence of organisms in contagious products. As vaccine and small-pox have been already mentioned, I will refer to that subject first.

The earliest published observations as to the existence of micro-

* See *London Medical Record*, November 19th, 1873.

phytes in the infective liquids of vaccine and small-pox were those of Hallier and Keber (1868), both of which were made with bad instruments, and attracted less attention than they would otherwise have done from the speculations with which they were associated. My own description of the organisms of vaccine appeared in an appendix to the Twelfth Report of the Medical Officer of the Privy Council in 1870. About the same time, but quite independently, they were much more completely investigated by Cohn, the eminent professor of botany at Breslau.* The description of Cohn agrees entirely with mine: a fact which I think important enough to mention, on account of its bearing on certain statements recently published by Dr. Beale, to which I must refer immediately.

Cohn has given to the organism seen in vaccine the designation of *Microsphaera Vaccine*. In fresh vaccine, it consists, according to his description, of minute spheroids grouped in couples or isolated. If a preparation of lymph be observed under the microscope on the warm stage, these particles divide repeatedly, and thus resolve themselves into chaplets. By this fact, as well as by their chemical reactions, they are easily recognised as micrococci. There is, I think, no particular reason to doubt the accuracy of the observation, discovered as it was in the first instance by observers working quite independently of each other, and in ignorance of each other's results. I was, therefore, rather surprised that, in a recent work on *Disease-Germs*, Dr. Beale should have criticised my very brief description of these organisms, and particularly the woodcuts with which it is illustrated, in such strong terms as he has employed. I cannot show you my woodcut, but I have placed before you a copy of Cohn's drawing made by a draughtsman. I have also placed on the board an exact representation of Dr. Beale's drawing of the particles in vaccine which he distinguishes as "true disease-germs", in contrast to mine, which he regards as false ones. Be it remembered that I have not asserted that the particles in question are "disease-germs" at all. All that has been stated is, first, that they are independent organisms, and, secondly, that they are to be observed in fresh vaccine.†

Shortly before the appearance of Cohn's first paper, another Breslau observer—a pathologist and hospital physician, not a botanist—published a short communication founded on the microscopical examination of the skin in persons who had died of small-pox, in which he stated that he had found the lymphatic vessels of the cutis plugged with a granular mass which exhibited all the characters of micrococci. These lymphatic vessels were met with for the most part in the tissue of the corium underneath and around pustules in various stages of advancement. Here, in some cases, they occurred so constantly, that they could be found in every vertical section of the skin which comprised a pustule, though they were absent in others.

This statement being founded on a considerable number of cases, is probably well worthy of confidence. It is to be noted with respect to it, that the appearances in question were observed only in cases which terminated early in the disease, *i.e.*, before the seventh day. In more advanced cases, the infiltration of the tissues and the consequent impletion with the cellular products of inflammation, rendered it impossible to make out with certainty whether the vegetations were present.

The two facts you have before you, *viz.*, the existence of organisms in vaccine matter, and the occurrence of similar organisms (not ascertained to be identical with the other) in the lymphatics, suggest the probability of their having to do with the morbid process, but cannot be accepted as an adequate proof that they possess the property of reproducing or propagating the disease. For the establishment of such proof with respect to any contagium, it would have to be shown either that when deprived of its organisms, though otherwise unal-

tered, it is deprived of its activity; or that when the organisms are introduced alone, they manifest the contagious property of the liquid or tissue from which they were derived. An imperfect approach towards the first of these demonstrations was made in Chauveau's experimental investigations; for it was shown that many contagious liquids lose their activity when they are deprived of the suspended particles in which whatever organisms they contain are included. The second demonstration must, with our present means of observation, be regarded as impossible, on the ground that the bodies in question are so minute that there is not the slightest prospect of our being able to separate them in anything like purity.

Another reason why no method based on the separation of the living contagious particles could possibly be successful is, that the particles themselves, if removed from the conditions adapted to them, would in all probability, as a direct consequence of that change, entirely alter their properties. Even organisms much higher in the scale, for example, many plants containing active principles, become inert when removed from an appropriate to an inappropriate soil. Much more, therefore, should we expect a similar result in the case of organisms, the vital processes of which are so much more under the influence of conditions.

Considering these difficulties, I set myself last year to consider whether there might not be methods of investigation within reach, which, if they did not come up to the strict requirements of the problem, might help us to approach it. If, it occurred to me, in any disease capable of propagation by the insertion of a contagium containing recognisable living organisms, however minute, it were in our power to observe the behaviour of these organisms during and after the act of infection, even if it were impossible to separate them from the contagious liquid or substance along with which they were introduced into the body of the infected person or animal, we should be able, by comparing the transformations or other manifestations of vital activity in the lower organism or parasite, with the functional derangements and textural changes in the higher organism resulting from the infection, to ascertain with the utmost precision the nature of the relation, if any, between the two series of phenomena. If this method could be carried out, I thought it might be anticipated with great certainty that it would be possible by means of it to determine in the particular case, that the one process is or is not the efficient cause of the other.

As regards many infective or contagious diseases, the application of such a method would be impossible, for we have no sufficient knowledge either of the door by which the contagium enters, or of its whereabouts in the organism after its entrance. In the case of small-pox these difficulties do not exist; and of all human contagious diseases it is theoretically the most fitting for such an inquiry. We have the virus, we have the organism, we have the process. We know how the virus enters. We know how it is scattered over the surface as thistle down is scattered over a field; and how each seed sown serves as a centre of origin for a morbid process, complete in itself. If we could—imitating Dr. Weigert's method, but carrying it out much further than he did—not merely search for our organisms at the sixth day, but at each successive period in the local process, from the first sign of functional disturbance in the rete Malpighii at the seat of the future papule, to the maturation of the pustule, and could trace the two developments—that of plant-life life on the one hand, and that of pathological and structural change on the other—going on side by side; and, as has been already explained, see that both were correlative manifestations of the same action, the object would, as regards small-pox, be accomplished.

But here we are met by an insurmountable practical difficulty. No opportunity is ever likely to be afforded us of investigating the pathological anatomy of small-pox in those early stages, about which it is most important to obtain information. Happily, comparative pathology affords us a means of circumventing this difficulty. In the sheep there is a disease which, as regards its origin, progress, and local manifestations, is the very counterpart of human small-pox.

The virus of sheep-pox, as I had the opportunity of observing in 1869, contains organisms similar to those of small-pox and vaccine. The analogy, therefore, is complete—so complete, indeed, that whatever can be ascertained by observation as to the behaviour of the organism of sheep-pox within the body of the infected animals, might be applied with the greatest confidence to the elucidation of the corresponding processes in human disease. On these grounds, I suggested to the Chief of the Medical Department of the Government that my colleague at the Brown Institution, Dr. Klein, should be requested to undertake an anatomical investigation of the disease, for which I was enabled to obtain material through the kindness of Professor Chauveau of Lyons and Professor Cohn. The results have been already communicated to the Royal Society, and will shortly be published in the *Philosophical*

* The reader will find a full account of these investigations in a prefatory paper entitled *Recent Researches on the Pathology of the Infective Processes*, in the first of the series of scientific contributions about to be issued by the Medical Officer of the Privy Council. It is expected that the first number will be out in a few days.

† For the information of the reader, I transcribe the passage referred to. "The drawing given by Dr. Sanderson conveys no idea of the actual appearance of the matter represented. A few minute circles may be made to indicate very fairly the appearance of microscopic fungi; but they are no more like the particles of vaccine lymph, or any contagious poison, or any kind of living matter known, than an oil-globule or an air-bubble is like a white blood-corpusele or a pus-corpusele. Such illustrations only help to retard investigation, and to convey erroneous ideas regarding the character of the matters referred to" (*Disease Germs*, second edition, p. 237). There can be no doubt that my drawings are not like those of Dr. Beale; but that they give a true notion of the objects represented, the reader may satisfy himself by comparing them with those of Professor Cohn: the resemblance between them is complete. No doubt Dr. Beale, regarding us both as "blind leaders of the blind", would find both representations alike faulty. The explanation of the discrepancy is obvious. I had before me certain spheroidal bodies of extreme minuteness, which I represented in my woodcuts in the usual conventional way—*i.e.*, by what Dr. Beale calls "minute circles". Professor Cohn's figures are of the same character. Dr. Beale had before him "bioplasts" of various shapes and sizes, all admirably drawn (see *Disease Germs*, fig. 66). It could hardly be expected that the pictures should be like each other.

Transactions, as well as in the forthcoming Report of the Medical Officer of the Government.

Before giving a short account of them, I must refer for a moment to well known facts relating to the development of the pustule in human small-pox. Each pustule must be regarded as what is called in pathology a focus of inflammation—an acute process which has a centre of origin. Where is this centre? If we refer to a diagram of the skin, as to a map, we fix the first localisation of the process at the junction-line between corium and epithelium, *i.e.*, between the structure called the rete Malpighii, and the very vascular layer beneath it which forms the papillæ. Let us consider what lies on each side of that line. Above it there are small cells, polygonal and closely packed—the growing cells of the epithelium. As you trace the stratum upwards, they flatten, then suddenly change their character and become horny. This we call the natural *stratum corneum*. Below the line referred to, there are papillæ composed of a dense but transparent tissue, so closely packed with loops of capillaries that, when these are distended, it looks as if it were all blood-vessels. Below this is a layer where there are fewer vessels, but they are still very numerous.

The anatomical changes in the structures of the corium and epidermis which result in the formation of the small-pox pustule have their principal seat and origin on either side of the well defined line, which, as I have just said, separates in a vertical section of skin the rete Malpighii from the vascular tissue of the papillæ. Above that line, the pathological processes consist at first merely in overgrowth—*i.e.*, in germination of the cells of the deep layer of the epidermis; but, as it progresses, two remarkable changes occur. Cavities (the future “vesicles” or “cells”) form in the Malpighian layer, which are at first full of clear liquid, afterwards of pus; and, secondly, the epidermis-elements appear to fuse together into a horny material. This horny material constitutes not only the covering of the vesicles, but the septa by which the adjoining cells are separated from each other; and it is by the shrinking which attends its formation that the central depression afterwards observed is produced. In the corium, on the other hand; the lymphatic spaces fill, the tissue swells, and thus the prominence or “papule” is formed.

In sheep-pox, the same changes take place; but they have been much more completely studied, as I have said, by Dr. Klein. To save time, I must carefully avoid all that, however interesting, is not essential. Let me draw your attention once more to the rete Malpighii and to the superficial lymphatics of the cutis. In the rete, there is at first a general germination. Then certain cells become distinguished as being larger; these expand by vacuolation; they become cysts. The cysts coalesce, and thus are formed cavities (the cells of the older pathologists) in the thickened rete. In the corium, we having filling out of the tissue by liquid which occupied the interfascicular spaces of the lymphatic network. Then (tracing the process further) we observe that, in the rete, the vesicles continue to enlarge, and their contents alter. Instead of containing clear liquid with granules, they are full of pus-corpuscles. In the corium, the change is of the same nature, but goes on earlier; the whole tissue becomes inundated with leucocytes.* This inundation begins from the lymphatics, the appearances being such as to suggest an obstruction or blocking up of these vessels. Rapidly the tissue of the corium becomes fuller and fuller of corpuscles, the final act being the extension of the cellular inundation to the rete Malpighii. How do they get there? They are certainly not formed in the vesicular cavities. Dr. Klein has no doubt that they migrate into the vesicles from the papillary layer below, by virtue of their amœboid movements.

As yet I have said nothing about the organisms. It will be remembered that Dr. Weigert found them only in the early stage of the pustule of small-pox; so here it would be in vain to look for them in the stage of suppuration. With this consideration in mind, Dr. Klein devoted his whole attention to the early changes. I may as well state at once that the anticipation that the early stages of the papule would be accompanied by the development of vegetation has been realised. The process has been studied both in the primary inoculation-pustules and in the general eruption, with results which may be thus stated. From the first, the cavities in which liquid collects, whether the lymphatics of the corium or the vesicular cavities of the skin, begin to show indications of containing organic forms. As the process is observed in sections made at various stages, its nature becomes more and more manifest. At first, it might be said, “Oh, these are merely the ordinary septic organisms with which we are familiar”. Soon, however, this becomes impossible. First, the form which is most cha-

racteristic—that of the *rod*—is entirely absent. Secondly, the stage of the process is not that at which ordinary septic bacteria present themselves. In all infective inflammations, when they assume the destructive character, bacteria may appear in the inflammation-products, but they never appear in the early stages of the process.

Then, finally, the development of the vegetations, whether it was examined in the primary pustules or those of the general eruption, whether in the corium or epidermis, presented everywhere the same characteristics—characteristics which differed entirely from anything we have up to this moment had under our consideration. It consisted in the formation of a felt-work of extremely delicate filaments, which, although they were not jointed, were unquestionably branched, and gave off at the growing ends minute acrospores or conidia, after the manner of the fungi of the penicillium group. These *mycelia* were first discovered in the initial stage of the disease in the lymphatics. Although the most scrupulous precautions were used—the portions of skin examined being plunged in the absolutely fresh state into alcohol—the fact was so strange, so unexpected, that it could hardly be credited. Whatever doubt, however, existed, was at once removed when it was found that the development was repeated in the “cells” or vesicular cavities of the epidermis, the same forms exactly presenting themselves; and the intimate relation of the whole process to the disease was rendered still more certain when it was observed that, on the appearance of the secondary eruption at the tenth day after inoculation, each of the small papules was an epitome of the large one, not only as regards the structural changes, but also as regards the evolution of plant life which was associated with it.

[In the remaining portion of this lecture, with which the subject will be concluded, were noticed the results of recent researches regarding the only other diseases in respect of which a definite relation between contagious processes and specific forms has, as yet, been made out, *viz.*, relapsing fever and the splenic fever of cattle.—J. B. S.]

ON THE APPLICATION OF COTTON-WOOL TO THE MEATUS AUDITORIUS.

In the JOURNAL of January 9th and February 20th, correspondents accuse cotton-wool of being injurious to the ears; and they seem acquainted with only this, the smallest (and avoidable) portion of its effects. It is true that, if dry cotton-wool be pushed *far* into an ear whose cutaneous lining is already in a congested or irritable condition, it will most likely do much more harm than good. The value of cotton-wool, properly employed, in cases of otorrhœa and perforated or lost membrana tympani, is beyond price, and none the less real because not in vogue with German aurists, who somehow seem to have adopted modifications of Toynbee's India-rubber artificial membrane, rather than Yearsley's cotton-wool substitute. In England (and in America too, I believe), the preference is quite the reverse; and I should say that, in this country alone, there must be hundreds of persons who are daily introducing and wearing these little pledgets of cotton-wool, pushed home against the remnants of their “drums”, not only without the slightest inconvenience, but with immense benefit. I know of a goodly number myself. As a rule, these dossils are not introduced dry, but saturated with plain water, glycerine, oil, or other fluid, according to circumstances; and it is a good plan to remoisten before withdrawing them, if they have been in any time. I see that the ear-fungus from which D. McD. suffered is said by one German aurist (Bezold) to be caused by the use of olive-oil; but, if that be so, one would think that the parasite would more frequently be met with than it is.

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POISONING BY BICHROMATE OF POTASH.

A PHOTOGRAPHER in this neighbourhood recently drank a quantity of a strong solution of bichromate of potash, having mistaken the jug for another which contained ale. I found him very prostrate, sweating profusely, and complaining of severe abdominal pains. He was also slightly purged, the evacuations being of a greenish-yellow colour. The pupils were dilated, and the pulse very weak and fluttering. I administered sulphate of zinc in water two or three times, until vomiting and active purgation had been induced. Subsequently, olive-oil was given him. He remained very weak for some time, and the stomach could only tolerate the mildest food.

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* From an abstract just received of Dr. Weigert's further researches on small-pox, it appears that the migration of leucocytes takes place in the pustule of this disease in the same way as above discussed in sheep pox.