LECTURES ON THE INFECTIVE PROCESSES OF DISEASE.

Delivered in the Theatre of the University of London.

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LECTURE III.—*Pathology of Septicæmia (continued).*

I WILL now ask you to allow me to bring together the conclusions at which we have up to this point arrived, in order that we may ascertain what is still required to enable us to understand the relation between the process of putrefaction as it is known to the chemist and physicist, with its morphological accompaniments, bacteria, and the pathological result in which we are so much interested, septicæmia. We have seen, first, that the septic virus is exclusively a product of the vegetation of bacteria—that it can no more come into existence independently of these organisms than the ferment* or enzyme of the stomach or pancreas can be formed without the secreting structures to which each belongs; secondly, that the bacteria which so generate the virus are incapable of carrying on or continuing the process in the healthy human or animal organism; and finally, that the most important pathological effects of septic poisoning may be explained and accounted for on the supposition that it determines the disintegration of the leucocytes of the blood. We are now prepared to examine another set of facts which have a bearing on the question of the alleged pathogenic action of bacteria; namely, those which show what happens to those organisms when, by accident or design, they find their way into the tissues or the blood. It is not until we have done this, that we shall be in a position to form an opinion in how far we are justified in speaking of them as causes of disease.

Four years ago,† we fully considered the question of the channels by which bacteria enter the animal or human organism. We then saw what an open doorway the absorbent apparatus of the mucous membrane of the small intestine affords for the purpose. I placed before you the experimental proofs that bacteria certainly do enter the organism constantly by the lacteals, and also by the pulmonary mucous membrane. That they enter the healthy body in any other way, cannot be asserted. It may, however, be considered certain that they may enter by any recent wound or traumatic surface, as, for example, by the uterine surface after delivery. I also brought before you experiments showing that, in the healthy state of the animal body, the circulating blood never contains septic bacteria or their germs; the proof being that it is always possible, if blood be received from an artery or vein into a calcined tube, to preserve it without putrefactive change for an indefinite period.

I will take these facts as proved, and content myself with corroborating the evidence they afford by new ones bearing on the same subject. In order to make it perfectly clear that bacteria or their germs may exist in the animal body without in any way interfering with health, I will refer to an experiment which I have several times made.‡ It consists in killing a healthy animal (a rabbit) and rapidly opening the abdominal cavity, cutting out the liver and kidneys with perfectly pure instruments, and allowing each organ to drop without a moment's

* In order to get rid of the confusion which often arises from the employment of the word "ferment" in different senses, Kühne proposed, in the first of the elaborate series of papers he has lately published on the action of the digestive ferments, to designate "the unorganised ferments, which act in the absence of organisms"—enzymes. See Kühne, "Ueber das Verhalten verschiedener organisirter und sogenannter Fermente"; *Verhand. der naturhist. med. Vereins zu Heidelberg*, 1876, p. 190.

† See BRITISH MEDICAL JOURNAL, February 13th, 1875.

‡ It is necessary to explain that this mode of investigation is not mine. The method was employed by Dr. Tiegel in Professor Kühne's laboratory in 1874, and described by him in a paper in the 6th volume of Virchow's *Archiv*. He investigated not merely the liver, but the pancreas, spleen, salivary glands, lymphatic glands, and other organs; but it was in the three first mentioned that he obtained the most conclusive proofs of fertility. About the same time, similar observations were made by Professor Billroth, of which an account will be found in his work already quoted (*Coccobacteria*, pp. 26, et seq.). In my own experiments, made in 1874, I followed Dr. Tiegel; but in repeating them, with the kind aid of my friend Dr. Roy, last autumn, I adopted what I thought a better method.

delay into a basin previously prepared, containing fused paraffine at the temperature of 110 deg. C. (230 deg. Fahr.) As soon as the mass has solidified, its surface is covered with Venice turpentine, in order to provide against the possibility of contamination by the cracking which is apt to occur in cooling. In some instances, the experiment was varied by substituting oil at the same temperature for the paraffine. Whichever of these plans is adopted, the organ, be it liver, kidney, or heart, by its greater specific gravity sinks to the bottom. If, after a day or two, it be removed and cut into, it is found that its internal surface is firm and opaque, in consequence of the action upon it of the hot paraffine or oil, but that the interior still retains its red colour, a proof that, notwithstanding the very high temperature of the paraffine, that of the central kernel of the immersed organ can never have much exceeded the coagulation point of albumin. Under the conditions I have described to you, it seems to me quite impossible to suppose either that germs could penetrate to the organ from the outside, or that any germ encountered by the organ in its transference from the body of the animal to the basin, could escape destruction. If, therefore, bacteria be found, they or their germs must have been there before the organ was plunged into the hot liquid.

The results of all the experiments, whether with liver or kidneys, was the same. The soft red kernel of uncooked tissue at the middle of the organ always contained bacteria, the vigorous development of which was indicated by their large size, countless numbers, and active movements. To my own mind, the experiment is conclusive. It proves that, in each of the organs experimented on, germs were present during life. If this be so, why did they not grow and multiply? I believe that the question cannot be answered consistently with the germ-theory,* provided that theory is to be understood in the sense in which I stated it to you at the beginning of this lecture. If it be said that the animal is a rabbit, and that you cannot argue from a rabbit to a human being, I answer that only increases the difficulty; for it is certain that under pathological conditions bacteria grow with great facility, not only in the tissues, but even in the blood of these animals. If, therefore, it be true that septic germs are capable of developing at all in the healthy organism, they ought to develop with special facility in the bodies of rodents; for it will hardly be suggested that, if these animals had not been killed, the germs which were present in their livers would have germinated. There are, therefore, two possibilities open to us. What is observed is (1) that by means of the portal circulation, germs must be continually entering the general blood-stream; and (2) that no bacteria exist in the circulating blood, or at all events only a stray one here and there. The alternatives are: either that the bacteria are formed and are immediately afterwards destroyed (for no provision exists in the organism for their elimination), or that they are not allowed to germinate, i. e., that the conditions under which they are placed in the living organism are such as to prevent their development. The question, which of these alternatives is the true one, I shall not attempt to answer definitively. There are, however, considerations which seem to me to render the first of them more probable than the second. Certain recent and extremely beautiful experiments of Professor Tyndall have shown that comparatively low temperatures, when discontinuously and repeatedly applied, *coup sur coup*, have the power of gradually destroying the germinating power of a liquid, i. e., of rendering it sterile. Now, evidently this is a case which resembles that of the germs continually delivered into the blood-stream of a living animal. Professor Tyndall explains it by supposing that a period of latency intervenes between the germ state and that of the finished organism, during which the germ particles are being prepared for their emergence into fully-formed bacteria. The same thing may very possibly happen in the organism. The germinal material may be allowed just to spring into activity in order to be at once destroyed. The reason why I think this probable is that, when I collect blood (with the precautions that were so admirably described to us last night at the Pathological Society), I find, as Mr. Lister and others have found, that it is sterile. I must, therefore, suppose that germs are not normally present in the blood. Now, inasmuch as material which has been proved by experiment to be so extremely resistant, as germinal stuff has been shown to be by Professor Tyndall's experiments, is not likely to be destroyed while in the germ-state in the circulation, it is not at all improbable that its fate is comparable to that of the germs which are destroyed by the discontinuous application of heat. It is allowed to live in order that it may die.

All of this, of course, is mere speculation. We have no means of observing what happens. The one fact that is certain is, that the

* See the enunciation of the "germ-theory" at the beginning of the lecture. I am well aware that it is possible to attach great importance to the exclusion of germs, without holding the extreme view that the intrusion of a single septic germ, or of any moderate number of them, can of itself be the determining cause of disease.

common septic bacteria cannot live in the circulating blood of a healthy animal. Why is this? Various explanations have been given of it. It has been attributed to the alkalinity of the blood, to the want of oxygen, to the excess of oxygen, to the struggle for existence between the blood-corpuscles and the bacteria. The suggestion that it is due to the excess of oxygen is groundless; for in the circulating blood the quantity of free oxygen present is not more than a quarter of the quantity that can be pumped out of this same volume of water freely exposed to the air.* Nor is it dependent on defect of oxygen; for recent experiments have shown that bacteria continue to vegetate, though slowly, in the entire absence of oxygen. As regards the third suggestion, that bacteria are destroyed in the struggle for existence, it is difficult to criticise it till we know what is meant. I confess I do not understand the analogy which is implied in the expression.†

In connection with the fact that germs are met with in the liver and other abdominal organs, I would remind you of another which clearly stands in relation with it: the observation which has been referred to by Dr. Bastian in his published writings (and was adverted to by him in his observations at the Pathological Society last evening), that, in peritoneal and pleural inflammations in rodents, however produced, it invariably happens that the exudation-liquids contain swarms of bacteria.‡

There are two cases in which this result presents itself: the first, in which in the course of a general infection, which may happen to be of a specific kind, the serous membranes become secondarily inflamed; the other, in which a traumatic inflammation is produced by the introduction of a drop or two of an irritating liquid. If this liquid be, as in the original experiment, itself a germicide, it is clear that no germs can come from outside with it. Obviously, here you have virtually an occluded wound, in which a traumatic inflammation is set up of an infective character. I do not doubt that the germs in this case come in from the intestine; but it is no less certain that they would be utterly harmless, unless the substratum for their development existed in the development of the inflammatory process.

I will conclude by drawing your attention once more to an experimental fact, to which, if I mistake not, I adverted to in my Lectures of 1873. I refer to an experiment made by my friend, Professor Chauveau§ for the purpose of illustrating the influence of blood-contamination—in short, of the septicæmic state—as the progress of traumatic inflammation. It is well known that, among the many operations which are daily inflicted on animals for the purpose of adapting them to the requirements of human luxury, there is one known as *bistournage*, which is largely employed in certain countries. This consists in twisting the spermatic cord, without making any external wound, in such a way that the circulation in the organ is permanently stopped. Of the thousands of operations of this sort which are daily performed, none are ever followed by infective consequences. The organ becomes encapsuled, and eventually shrivels. But if, previously to the operation, a dose of septic matter have been introduced into blood-stream, what happens then? The textures around the organ become the seat of acute diffuse inflammation, which soon extends to adjoining parts, and may threaten life. What is the meaning of this? In the thousands of animals that undergo *bistournage*, without suffering from it, the result is but a counterpart of what happens in a wound when entirely protected from contamination. In the single case, which is infected, a poison present in the blood-stream determines in the injured part an infective inflammation. The experiment affords a striking instance of

the co-operation of two agencies in one pathological process; both of which agencies, although not affecting the result with equal directness, were alike essential. The immediate cause of the septic inflammation of the testicle was evidently the injury to which it had been subjected; but no infective process would have developed itself—nay more, no inflammation whatever would have occurred—had it not been that masses of septic matter were at the time of the injury circulating in the blood-stream, some of which were conveyed to the injured part, and then became centres of infective action.

On the other hand, the constitutional effects which were produced by the injection of the septic liquid into the blood would have passed off without endangering the life of the animal, if there had been no injured organ to afford the necessary conditions for the development of a septic focus. Two causes, therefore, were concerned: the injury and the septic particles which were brought to the injured part by the blood-stream; and of either it could be stated, with equal truth, that it would not have been efficient without the other. In this respect, the *bistournage* experiment admits of the same explanation as the one previously mentioned, in which a septic peritonitis was induced by the injection of a drop or two of solution of iodine into the peritoneal cavity; for, in the one case as in the other, the injury which was the immediate cause of the pathological process would have had no infectious results, unless infective particles had been present. But here the parallelism ceases; for, by a further experiment, Chauveau showed that, if the septic liquid were carefully filtered before injection, so as to deprive it of its visible particles, *bistournage* could be performed without unfavourable result. The filtrate, though obviously still contaminating, was quite innocuous. It appeared to be essential to the morbid fruitfulness of the seed sown that it should be enclosed in particles of sufficient size to lodge in the capillaries of the injured part.

[To be continued.]

LOCALISATION IN SPINAL DISEASE:

ILLUSTRATED BY (1) A CASE OF "ATROPHIC PARALYSIS" IN AN ADULT; (2) A CASE OF CENTRAL MYELITIS; (3) A CASE OF ALCOHOLIC PARAPLEGIA.

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WE are indebted to the labours of Lockhart Clarke, of Duchenne (de Boulogne), of Charcot and his pupils, and other observers, for the knowledge that the spinal cord, though so narrow in its lateral dimensions, yet presents a special localisation in different districts, under the influence of disease, almost, if not quite, as distinct as has been observed in diseases of the brain. Several districts in the cord can be mapped out by the phenomena of disease, some of them equally distinct in their functional endowments, and some in the different periods in which they undergo development during foetal existence. Among these districts, particular interest attaches to the central grey matter, and especially to its anterior and posterior cornua; these cornua presenting a remarkable distinctness in the diseases to which they are subject, as much so as in the functions to which they are respectively subservient.

A large and important group of maladies originates in morbid changes taking place in the anterior cornua, and belongs in essentials to these cornua, the implication of neighbouring tissues constituting a secondary and subordinate process. This group has been classed by M. Charcot under the title of "myopathies spinales". In the maladies by which it is constituted, whether acute or chronic, the distinguishing characteristic is, that the transmission of sensitive impressions is not modified at all, or only in a secondary and subordinate manner. The entire stress of the disease falls upon the motor function and the nutrition of the muscles. Voluntary motion is more or less enfeebled; but what localises the paralyzing influence in the anterior horns is the muscular atrophy by which it is attended. As is well known, the atrophy in some of the diseases reaches the extent of entire destruction of the muscle affected.

My first case belongs to the acute variety of this group. It is intimately related to a well-known malady, "atrophic paralysis of infancy": a disease in which the morbid changes commence in the anterior horns of the spinal grey matter, and, according to M. Charcot, are usually restricted to one or two of the circumscribed oval groups of large ganglionic motor cells characterising those horns. These cells form the starting-point and centre of the morbid process, and it is only in the utmost stage of alteration and in certain regions that the horn is invaded through its entire extent. (*Leçons*, 2me série, p. 181.)

* The quantity of free oxygen in common water exposed to the atmosphere is about 0.6 per cent. per volume at ordinary temperature, that of oxygen in the blood about 0.15. The extreme smallness of the quantity of free oxygen in circulating blood is due to the presence of a body (hæmoglobin) which seizes upon the oxygen with great avidity. On the other hand, there can be no doubt that the oxygen present in the blood is sufficient for the maintenance of bacterial life; for in the experiments recently conducted under Professor Donders' supervision at Utrecht, it was found that although oxygen, as is well known, promotes the vital activity of bacteria, these organisms can live in its absence—a fact explained by supposing that they have the power of tearing it from other combinations. See Grossmann and Mayerhausen, "Ueber das Leben der Bacterien in Gasen"; *Pflüger's Archiv*, vol. xv, p. 245.

† Since delivering this lecture, I have become acquainted with a paper by P. Granitz ("Experimentelle Untersuch. über die durch Parasiten bedingten Krankheiten"; *Virchow's Archiv*, vol. lxx, p. 546), in which the author adduces several striking facts in support of the conclusion that, just as the vegetative processes of the fungi are checked whenever they are brought into competition with those of more vigorously growing organisms, so the growth of ferment organisms is restrained in presence of actively growing cells—e.g., pus-corpuscles.

‡ On the same occasion, Dr. Bastian referred to another fact of a similar nature—namely, that when by the injection of irritant liquids under the skin an inflammation of the subcutaneous tissue is produced in rabbits, the exudation liquids are found to swarm with bacteria. The explanation is, that the skin at the injured part being infiltrated with exudation, is no longer protective. Its external contaminated surface is thereby brought into relation with the subcutaneous tissues.

§ Chauveau, "Etude expérimentale sur les phénomènes de mortification et de putréfaction qui se passent dans l'organisme animal vivant"; *Bull. de l'Acad. de Médecine*, 1873, p. 540.