LECTURES ON THE OCCURRENCE OF ORGANIC FORMS IN CONNECTION WITH CONTAGIOUS AND INFECTIVE DISEASES.

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BY

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LECTURE III.—(Continued.)

THERE are two contagious diseases besides small-pox, in respect of which there is reason to suppose that specific organic forms exist either in the blood or in the affected tissues: namely, relapsing fever and splenic fever. I propose to take splenic fever first.*

Splenic fever is a malignant highly contagious disease of cattle, distinguished by the extreme rapidity of its course and fatal termination. It is interesting to us on account of the fact that it is characterised by the existence in the blood of organisms which, from the investigations of trustworthy observers, seem, though like common bacteria in form, to have such marked peculiarities of their own, that they may be regarded as specific. These bodies were discovered in 1855, or perhaps earlier; but their significance is still matter of dispute, there being great difference of opinion (even among those who admit that they are characteristic of the disease) as to the part they play in the morbid process.

The disease may be communicated by any means which involves the transference of a portion of the blood of a diseased animal to the living tissue of an animal previously healthy. It is not known that it can be propagated by any other way; for animals kept in the closest proximity to diseased ones, and placed under the most favourable conditions for infection through the air, are not infected.

The most striking feature of the disease is its extremely rapid progress and its short duration: in the so-called apoplectic cases, a few hours; in the more ordinary ones, a day or two. A sketch may be given in a few words of the disease as it presents itself in acute cases in cattle. An animal, which perhaps for the previous day has declined food and shown signs of general disturbance, begins to shudder and to have twitches of the muscles of the back, and soon afterwards becomes weak and listless. In the meantime, the respiration becomes frequent and often difficult, and the temperature rises to three or four degrees above the normal; but soon convulsions, affecting chiefly the muscles of the back and loins, usher in the fatal collapse, of which the progress is marked by complete loss of power of moving the trunk or extremities, diminution of temperature, mucous and sanguinolent alvine evacuations, similar discharges from the mouth and nares, and death. In the horse, the disease presents similar characters, but is much less acute. The local affection is more frequently recognised during life, so that the case is often recorded as one of "acute splenic tumour".

Of the phenomena revealed by dissection, those which relate to the blood, to the circulatory and lymphatic systems, and to the spleen, are by far the most important. In the blood, the colourless corpuscles are increased, especially in the horse. In the mucous membranes, general infiltration is one of the most marked results of the disease. In cattle it is excessive, and affects the whole course of the intestine, the cavity of which is found to be full of sanguinolent transudation. In the horse it localises itself in the stomach and duodenum, and presents itself in the form of circumscribed inflammatory tumours or thickenings of the mucous membrane. As, in these tumours, the inflamed tissue dies in the middle and sloughs out, leaving an ulcer, they are called carbuncles. The ulcers are called "typhous ulcers", and the whole disease in the horse is often designated "typhus".

The discovery that in the blood of animals affected with splenic fever rod-like bodies are found in the liquor sanguinis was first, I believe, made by Pollender, who, in the year 1855, described them as "fine, apparently solid, straight unbranched objects". He stated that they possessed no proper motion, differing in this respect from ordinary

bacteria, leaving the question of their nature, as well as that of their relation to the contagion of the disease, open. A year or two after the publication of Pollender's paper, Brauell published the first of his very extensive series of researches on the contagion of splenic fever, in which he not only confirmed Pollender's discovery, but, by experiments in which he communicated the disease to animals under a great variety of conditions, acquired for pathologists the greater part of the accurate knowledge they now possess on the subject. He contented himself, however, with demonstrating that the organisms found in the blood in splenic fever were characteristic of the disease, without maintaining that they were, or that they were not, the *causes* of its virulence; and, indeed, was disposed to attribute more importance to them as diagnostics than as agents in the morbid process.

Three years later, the bodies in question were rediscovered by Delafond and Davaine, who, in claiming a priority which did not belong to them, no doubt did so in ignorance of the good work that had already been done in Germany. The existence of the rods as a characteristic of the circulating blood in animals affected with splenic fever, is a fact now admitted by all pathologists who are conversant with the disease. It is, however, remarkable (and at first sight difficult to understand) that many observers have expressed doubts as to their being organised living beings. Thus, Leisner at first took them for fragments of fibrin or for bits of tissue; others thought that they were blood-crystals. The statement made by Professor Bruckmüller of Vienna, and repeated by others, that Virchow at one time regarded the bacteria of splenic fever as blood-crystals, appears to be an erroneous one, founded on a misquotation of an oral communication.

The rods have been most carefully studied by Bollinger in his recent *Researches in Comparative Pathology*. Each rod is about as long as the width of a blood-corpuscle. Along with the rods spheroids can always be found, which are no doubt forms of the same organism—parts of the same continuous development. As regards their structure, examination with high powers shows that each rod is made up of spheroids, each spheroid consisting, like an ordinary micrococcus, of a central darker part with a more transparent envelope. The most remarkable fact relating to them is, that they disintegrate rapidly from the moment that the blood becomes putrescent. As they disappear, the actively moving rods and spheroids, which indicate the commencement of the septic process, take their place, but there is no continuity of development between the two kinds of organisms.

The principal source of doubt as regards the part played by the rods in the contagious process of splenic fever has been the observation first made by Brauell, that, in the early stage of the disease, no rods are found in the blood; and that nevertheless such blood possesses the contagious property. This question has been lately investigated very fully by Professor Bollinger, on the basis of experiments made expressly for the purpose. From the results of these experiments, it seems certain, (1) that blood without rods may yet be contagious; (2) that animals infected by it contain the rods in their blood in as great numbers as others. Are the rods, therefore, intimately associated with the contagious material—the contagium? or is their appearance a merely collateral phenomenon—a symptom of the disease?

It has been sought to answer this question in two ways: on the one hand, by separating the rods from the liquid, and determining their pathological properties by experiment; and on the other, by testing the activity of the liquid after the rods have been removed from it by some process of filtration. The first of these methods—that employed, or rather attempted, by Davaine and the French experimenters—has led to no result; and it is difficult to see how it could yield any; first, because complete separation of such organisms from the medium in which they are contained is impossible; and secondly, because, in the very act of filtration, the organisms themselves would probably undergo such changes as would entirely alter their properties. If, as is probable, the activity of the rods is dependent on their vital functions, there is no reason to anticipate that they would continue to manifest that activity when "out of their element"; still less that it would show itself in any descendants or progeny obtained from them by the method of cultivation. The other method has been used by Klebs and Tiegel. These observers have found that, just as it is possible to separate the bacteria contained in ordinary septic products from the liquid in which they are suspended by filtering them under pressure through a stratum of porous porcelain, the same method can also be successfully applied to blood containing the rods of splenic fever. The result of the experiments, which, it must be admitted, were not so frequently repeated as could have been wished, was, that the filtrate of blood (or rather the liquid of the spleen of a diseased animal), of the virulence of which experimental proof had previously been obtained, was found to be incapable of communicating the disease. Clearly, there is no proof in this fact that the contagium of splenic fever is exclusively contained in the

* The facts stated in this part of the lecture will be found in greater detail in the introductory paper already referred to contained in the Reports of the Medical Officer of the Privy Council on Scientific Investigations (New Series, No. III).

rods; but there is proof in it that the agent is, as we believe all other contagia are, a body which is incapable of solution or diffusion, and which attaches itself to concrete particles.

An additional and to my mind more satisfactory proof of this lies in the remarkable observation made by Brauell, that, when pregnant animals are affected with splenic fever, the blood of the embryo is not contagious. Brauell found in repeated trials that, in such animals, blood from the foetal circulation could be inoculated without result. Here the placental apparatus serves not merely as a filter, but as a diffusion-cell, keeping back not merely solid particles, but everything which is not capable of passing through animal membranes. This fact—of the immunity of the foetus—must be taken in connection with the incommunicability of the disease excepting by actual transference of blood.

★The contagium of splenic fever is wonderfully persistent. With reference to this point, there is an apparent antagonism of facts, which, however, on examination, turns out to be a perfect agreement. Brauell found that blood, after removal from the body, loses its activity in a few days. On the other hand, we are certain that the contagium must have a state of existence in which it is in the highest degree permanent and indestructible. Thus Bollinger gives an account of what may be called a stable-enzootic of splenic fever, in which ten cases occurred in one stable during a period of three years, no other cases occurring in the neighbourhood. The contagium must have remained latent during the whole period.

What does this mean? Here is a disease only transmissible by inoculation, and of very short duration. Why does it not perish out of existence? Clearly it would do so, had it not some as yet unknown means of perpetuating itself. How it does so, it would be too bold to conjecture. The rods can hardly be supposed to be the means of perpetuation; for, like the contagious property which they perhaps represent, they are very fugitive, and, in particular, like it and along with it, they disappear at the moment that putrefaction commences. It is, therefore, not possible to refer to them as contrivances suited for the storage of contagium, or for its conveyance to a distance, for either of which purposes they are obviously unfit. This very consideration, however, can, I think, be made to appear rather as an aid to our understanding of the relation between organisation, or rather living organic forms, and contagion, than as a difficulty or objection. For, if we turn from the specific form to what we know about the development and life-history of common bacteria, and, indeed, of the beings belonging to the same group in general, we find the same thing. Just as in the case of the specific contagium, we are compelled to recognise two states of existence, one enduring and latent, the other active, but fugitive; so among these organisms we find one condition in which the growth and multiplication of individuals is very active, but individual life is extremely short; another in which the vital activities of the organism are stored up for the future, the individual being for this very end endowed with the power of resisting external disintegrating agencies, and thereby of enduring for an indefinite period. Thus, without any effort, we find, in all probability, in the life-history and development of the organisms, the counterparts of all the phases of the process of contagion.

During the last few years, the pathology of splenic fever has acquired an even wider interest than it had before, from the publication of a series of cases of a rapidly fatal disease affecting the human subject which presents the characters of splenic fever, and turns out, on investigation, to be identical with it. The first of these cases was published by Professor Buhl at Munich in 1868. It was that of a man aged 32, who died after a short illness, of which collapse and vomiting were the chief symptoms. After death, the stomach and duodenum were found to be the seat of circumscribed foci of submucous infiltration, presenting characters similar to the so-called "carbuncles" of the intestine seen in the horse. The rods of splenic fever presented themselves in the blood, and the other lesions corresponding to those of the disease in question were found.

The affection was termed by Buhl "*Mycosis intestinalis*". Shortly afterwards, two other cases were recorded by Professor Waldeyer, now of Strasburg. In one of them, that of a slaughterer, whose occupation pointed to the sources of infection, the nature of the disease was suspected during life. After death, the suspicion was confirmed by the complete correspondence of the lesions with those of splenic fever in the horse. As in Buhl's case, the microscopical investigation showed that masses of zooglyca existed in the affected tissues, and that rod-like microphytes were to be found in the circulating blood, particularly in that of the portal vein. Other rapidly fatal cases have since been removed, all of which exhibited pathological appearances of the same kind, the most constant being the enlargement of the spleen and the circumscribed hæmorrhagic infiltrations of the intestines, resulting in

more or less extensive sloughing of the mucous membrane, and associated with serous exudations, infiltration of the subserous tissue, and hyperæmic enlargement of the lymphatic glands in relation with the infiltrated parts.

Whatever doubt remained as to the identity of mycosis intestinalis with splenic fever, was removed by the appearance of a communication by Dr. Münch of Moscow, who was able to state, from the results of his own dissections in the "Workman's Hospital" at that place, that in all the cases in which he had occasion to examine the bodies of men who had died of disease contracted by infection from animals, the intestinal lesions and the condition of the other internal viscera corresponded closely with those described by Buhl and Waldeyer. In these, as in many other cases recorded by the best observers, the primary pustule (*pustula maligna*) at the seat of inoculation, often supposed to be the one pathognomonic lesion of splenic fever in man, was by no means a constant feature. Out of twenty-eight cases recorded by Münch (1867-71), seventeen exhibited a primary pustule, which in all but two was carbunculous; but, in the other eleven cases, there was nothing whatever to be found on the skin.

As regards the morphological relations of the organisms found in mycosis intestinalis with those of splenic fever, further investigation is required. So far as the former have been described, they agree completely with the others, as may be readily seen by comparing the drawings of Wagner, taken from a case of mycosis, with Cohn's or Bollinger's representations of the rods of splenic fever.

The identity of the two forms being admitted, Buhl's and Waldeyer's anatomical investigations afford a key, which was before entirely wanting, to the understanding of the so-called "localisations" of splenic fever in cattle. This key consists in the demonstration that the formation of foci of infiltration, of which we read so constantly and repeatedly in the descriptions of the veterinary pathologists, is a process of which it is the characteristic that the tissues of the infiltrated part became infested by myriads of microphytes of a particular kind, so that the presence of these bodies is as much a part of the process as the emigration of the colourless corpuscles from the blood-vessels is a part of ordinary supuration. Further than this it is not possible to go, until the initial stages have been investigated in the lower animals.

I now pass to a disease which in two or three respects resembles splenic fever, while it differs from it in a great many more. As regards its mode of diffusion, there is this striking resemblance, that, although relapsing fever does not require inoculation in order to communicate itself from the sick to the healthy, the area within which its contagium can act is very limited. If a patient be introduced into a ward, the patient in the next bed may be attacked, but the disease does not spread. In the recent epidemic at Breslau, to which I am about to refer, there were many instances in which the disease found its way into rooms inhabited by several families, and it was then observed that the members of one family (in other words, those who lay on the same heap of straw) were attacked one after another, while the other occupants of the room remained exempt.

Another striking point of resemblance lies in this, that they are both pre-eminently blood-diseases. In the case of splenic fever, we have direct evidence of this in the fact that the disease is conveyed by transfusion of blood. Whether this is also true as regards relapsing fever has, of course, not been ascertained; but we have, as indications of the blood-affection, first, the fact that the spleen, of which the function is intimately connected with the blood, is enlarged in a similar way in both diseases; and, secondly, the fact which at the present moment specially interests us—the recent discovery that, in the blood of persons suffering from relapsing fever, organisms exist, which, from their remarkable form, are called *spirilla*.

During the prevalence of relapsing fever in Berlin in 1872, Dr. Obermeier, who had, in the previous epidemic of 1868, been engaged in microscopical investigation of the blood, announced the discovery of the spirilla in a communication made to the Berlin Medical Society. This communication was based on twelve cases, in all of which the organisms were observed. On March 26th, Dr. Obermeier published a second series of observations; twenty new cases had been investigated, in nine of which the blood had been examined daily. The results of these examinations showed, that the presence of the organisms in the blood was associated with the morbid process so closely, that as soon as the pyrexia disappeared they disappeared with it, reappearing when the patient again febrile in the relapse.

Soon after the death of Dr. Obermeier, a third series of observations was communicated by Dr. Engel to the *Berlin Medical Weekly Journal*, founded on the examination of the blood in eighteen cases in the Charité Hospital at Berlin, under the care of Professor Frerichs. They confirmed in every particular the statements of Obermeier, deriving additional value from the exact observations they contained as to

the time which intervenes between the onset of pyrexia and the first appearance of the organisms.

During the same year, the epidemic prevalence of relapsing fever at Breslau afforded additional opportunities for investigating the subject. The first results of these inquiries were communicated by Dr. Weigert to the Silesian Scientific Society on September 12th, 1873. The clinical relations of the subject have since been worked out by Dr. M. Litten in a report on the epidemic founded on observations in the General Hospital in Breslau.

In this report, Dr. Litten has given by far the most complete account of the spirilla that has yet been published. He confirms the statement of Obermeier that they are found only in the blood of persons affected with the disease. In more than one hundred cases they were never missed. They occurred only during the paroxysms, and invariably disappeared before the fall of temperature—never remaining during the period of apyrexia. Their number, however, varied considerably; they were sometimes so numerous as to crowd every field, at others they were difficult to find. Dr. Litten describes their motions as partly consisting in undulations which progress along the course of each fibril, and partly in oscillatory movements, *i.e.* alternate flexions and extensions, springing from some point in the course of the fibril.

Dr. Litten made some very interesting observations on the relation of these remarkable bodies to temperature. He observed that on raising the temperature of the stage of the microscope gradually to 60 deg. C., no effect was produced. As soon as this point was passed, the movements became languid. By the time that 65 deg. was reached, they had entirely ceased. No effect was observed on cooling the preparation to the temperature of freezing. When it was kept for some time on ice, the movements finally disappeared.

Here I stop. I have brought before you, to the best of my ability, the leading facts relating to the only four cases known to me in which the connection between organic forms and specific diseases has, as yet, been satisfactorily made out: those of cow-pox, sheep-pox, splenic fever, and relapsing fever. These four diseases, although they are so different, are associated by the fact that each of them presents very well marked nosological specificity—in other words, they are all of them characteristically contagious diseases. Small-pox we must not yet include, excepting on the ground of identity with cow-pox; but we may hope that the researches of Dr. Weigert, as soon as they appear, will afford us material for conclusions on this subject. In the meantime, let us carefully guard against undue precipitation, in the process of combining the few facts we are already in possession of into a system. The desire to discover the practical bearing of his results on the all important questions of prevention and treatment is a constant and ever recurring temptation to the scientific pathologist, seducing him from his path of patient and silent investigation into speculations about the origin and nature of disease which, even though they may sometimes lead to useful practical applications, have no permanent value.*

* Since this lecture was delivered, the first part of Dr. Weigert's Researches have been published at Breslau, with the title *Anatomische Beiträge zur Lehre von den Pocken*.

TREATMENT OF CLUB-FOOT.

I wish to call attention to a particular passage in Dr. George Buckland's paper on Club-foot, which deals with the "Non-cutting treatment." He says "A muscle of its (tibialis anticus) length, even when very rigid, can be stretched to a considerable degree: *if there are any cases of club-foot cured 'without cutting tendons'*, as some surgeons would have us believe, they must be trifling examples of the deformity, and the defect must depend wholly upon the long muscles of the leg, which is very rarely the case."

Mr. Barwell's method, in its entirety (shampooing, etc., mentioned by Dr. Buchanan, as well as mechanical means) has been adopted here during the past six months, by the advice of Mr. Wright, our senior surgeon, by whose kind permission and assistance, together with that of the staff generally, I have been enabled to collect a series of cases, the results of which I hope to publish at some future time. So far the treatment has thoroughly borne out all that has been stated by Mr. Barwell when advising its use. That there are cases of talipes, and the majority of such, which can be treated successfully by this method, our limited experience leaves no doubt. Dr. Buchanan lays great stress upon the early adoption of means for the cure of these deformities, and Mr. Barwell equally so; the success or non-success of treatment, in either case, depending mainly upon this; but, in the latter, it is also influenced by the amount of patience and perseverance possessed by the surgeon in whose hands the case may be.

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THE CROONIAN LECTURES ON ADDISON'S DISEASE.

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LECTURE III.

THE lesion in the suprarenal capsules in Addison's disease is produced, as I have shown, by an inflammatory exudation of low type with which these organs become infiltrated. This exudation becomes converted into a firm fibrous material, which first encroaches upon and destroys the normal tissue of the capsules, and subsequently itself, together with the destroyed elements of the organs, undergoes degeneration into purulent, cheesy, or cretaceous material. At first it would, not unnaturally, be supposed that this complete destruction of the normal structure of the capsules must be the immediate cause of the symptoms in Addison's disease; or, in other words, that these symptoms must result from the abolition of the proper function of those organs. This was evidently the opinion entertained by Addison when he published his book; for he expressed his belief that the urgency of the symptoms was determined by the actual amount or degree of morbid change going on in the capsules, and that, whilst universal disease of both capsules would probably be found to be uniformly fatal, cases in which the morbid change was limited to one capsule only might be found to be attended with proportionately slighter results. Since Addison's time, however, it has become generally recognised, by all those acquainted with the subject, that the symptoms associated with the suprarenal lesion cannot proceed from mere destruction of the tissues of the organs, and consequent abolition of their function. Many physiological experiments have been made upon animals, by Dr. Brown-Séquard, Dr. George Harley and others, with the view of deciding this point; but, looking to the differences in their results, and to the doubt how far these may have been due to accessory differences in the operative processes, I am disposed to attach much more weight to the clinical and pathological facts which seem to me to determine the question.

In my last lecture I showed, on the one hand, that when the normal structure of the suprarenal capsules is altogether supplanted by cancer, or has undergone complete fatty degeneration, none of the peculiar symptoms of Addison's disease are produced, notwithstanding the total destruction of the organs for all functional purposes; and, on the other hand, it is quite certain that, in many cases of Addison's disease, the conversion of the suprarenal capsules into a mass of fibroid tissue, and even the degeneration of this latter into cheesy material, must have been almost, if not altogether, complete before the development of any of the characteristic symptoms of the disease. In the case of the little girl, E. W., for example, the profound alteration in the capsules, more especially in the right one, which consisted chiefly of cheesy masses with some gritty matter bound together by translucent tissue, could not possibly have taken place to any extent during the brief period of her illness; and, in other cases in which the illness has been equally short, the capsules have been found in a still more advanced state of degeneration. Messrs. Rossignol and Little report a case of a servant girl, aged 15, whose illness had been noticed only four weeks before her death, and yet both suprarenal capsules were in a great part made up of material of a yellowish colour, like hard cheese, with here and there a little gritty matter; and presented no trace of normal structure. The paroxysmal mode of progress, characteristic of the usual chronic course of the disease, is also adverse to the probability of the symptoms being due to abolition of the function of the capsules, for, in that case, the frequent rallyings after severe paroxysms could scarcely take place, when the nature of the local lesion must render any renewal of function impossible. Again, in the case of other symmetrical organs, such as the lungs or kidneys, it usually happens that, if only one of the two organs is rendered functionally useless by disease, the other acquires an increased functional activity, termed compensatory; and, if life be not preserved, it is, at any rate, prolonged much beyond the average duration of life in cases in which both organs are diseased. In Addison's disease, on the contrary, in some of the very few cases in which one capsule only has been found to be diseased, the symptoms have,