LECTURES ON THE INFECTIVE PROCESSES OF DISEASE.

Delivered in the Theatre of the University of London.

By J. BURDON SANDERSON, M.D., LL.D., F.R.S.,
Professor of Physiology in University College; and Superintendent of the Brown
Institution.

LECTURE IV.—*The Germ-Theory, Contagium Vivum, Specific Infections.*

THE task I have set myself for to-day is one of considerable difficulty. I have two pathological theories to discuss, each of which has been the subject of much contention—the theory of contagium vivum and the germ-theory. In many persons' minds, these two theories are so closely associated, that they sometimes seem to be regarded as identical; yet, in reality, they have no necessary connection with each other.

By the expression *contagium vivum*, I mean to designate the doctrine that, when a contagious disease is communicated by the atmosphere, by personal intercourse, or in any other way, that conveyance takes place by specifically endowed organisms, which stand in a similar relation to the disease to that in which the seed does to the plant. For, just as the seed is at once the origin and offspring of the plant, so, according to this view, the morbid germ produces the disease, and is in its turn produced by it. This being understood, it is evident that the term contagium vivum relates exclusively to specific diseases, and therefore belongs mostly to medicine.

For a similar reason, the *germ-theory*, which relates to the inflammatory and other consequences of injuries, involves questions which are almost exclusively surgical. That theory teaches that certain organised and living particles of extreme, if not ultra-microscopical minuteness, which are always suspended in the atmosphere, are in such sense the causes of the suppuration and other destructive changes which interfere with the healing of a wound, that (1) if these organisms are excluded, the wound must enter at once on the processes of reparation, and (2) that if these organisms are present, it cannot so heal; and consequently that the whole secret of the successful treatment of wounds consists in the exclusion of that finest form of atmospheric dust which, whatever be the size of its particles, has been identified, as well by physicists* as by mycologists,† with the contaminating agents in question.

Let me begin by expressing to you, with all due respect, but not the less decidedly, my own personal conviction as to the value of the method of treatment of wounds which is, or professes to be, founded on the germ-theory. It may be said that it is no part of the business of a mere physiologist or pathologist to have any opinion on a practical question. But the present case is entirely an exception. The results are so patent, so conclusive, that it would be as reasonable to doubt of the utility of vaccination as of that of the anti-infective treatment of wounds. The fact that infective action can be prevented in a wound is established with as much certainty as any other pathological fact of which we have gained knowledge by experience. Indeed, if it had been possible to contrive and carry out a series of experiments for the mere purpose of testing it, we could not have had better proofs than have actually been afforded by hospital practice. We are able to compare what *is* under the improved methods, not only with what *was* before they were introduced, but with what still presents itself, where that "clinical precision", which is the soul of what I may venture to call the new surgery, has not as yet asserted itself.

I have recently been in Germany, and have had the opportunity not only of hearing the opinions of the leading pathologists in that country, but also of seeing some of the practical benefits which the adoption of what they call the "*Listersche Behandlung*" is accomplishing in that country. It is little more than three years since Professor Volkmann of Halle was led to try the antiseptic method. The results of his first experience of it were brought together in the form of a discourse which was delivered before the Surgical Congress at Berlin in 1874. In this dis-

course, he pointed out in the clearest way that the question whether the germ-theory was true or false ought not to have the slightest influence on their minds; that the question was one to be settled merely by experiment—and by experiments of the most agreeable kind—those, namely, in which the subject experimented upon himself derives his principal benefit. Is it the case or is it not the case that, in a wounded surface or an exposed serous surface, the reparative process will, under the influence of the antiseptic treatment, take place without the intervention of suppuration, and to the absolute exclusion of the subsequent destructive and infective processes? This was the question; and the affirmative answer which Volkmann gave, founded on the experience of fifteen months in the hospital of Halle, has been abundantly confirmed since. "In presenting these observations", he says, "I ask myself once more whether, in forming my opinion, I have kept myself uninfected by the prevailing fever" (by which he means what another great pathologist has called the bacterium craze—the tendency to attribute everything to bacterial influence). "I ask myself, and think I can answer, exclusively on the ground of clinical experience." It is quite unnecessary for my purpose, and it would be out of place here, to bring before you the details of Professor Volkmann's results, which can be read in the clinical lecture to which I have referred and in the author's more recent surgical contributions. I may, however, endeavour to communicate to you some impressions which I received in a recent visit to Halle. It is impossible to conceive a more favourable locality for making an experiment of such a nature; first, because the extraordinarily rapid progress of the manufactures of the town has rendered the hospital too small for its requirements, and consequently the proportion of severe cases (as I was able to observe in going round the wards) was very large; and secondly, because the hospital itself is not, perhaps, the worst, but *one* of the worst, that I have ever seen. Situated in the very centre of the town, overshadowed by a huge ecclesiastical building, and having for wards low rooms, each of which communicates with a latrine, and has its beds so close that there is scarcely more than room to pass between them, the hospital presents every circumstance likely to lead to the development of the worst traumatic affections. It is in such wards as these that compound fractures, amputations, and resections have been treated with a success which is up to the best results of London surgery. In a word, the influence of the most unfavourable conditions which can possibly be conceived (the disastrous effects of which were before so overpowering that, to Professor Volkmann, his clinical work had become a burden instead of a joy) have been simply neutralised by the conscientious carrying out, in all its details, with the earnest co-operation of the whole staff of the hospital, of the Edinburgh method.* Looked at from a pathological, that is from a scientific, point of view, the successful trials which have been made of Lister's treatment during the last few years in the great hospitals of Europe may be regarded as each a several experiment on a very large scale; the whole forming a series of experiments all of which point very distinctly to the same conclusion, that conclusion being, of course, that a serous surface may be exposed, and that living tissues may be incised, or even subjected to serious mechanical injury, without these parts becoming foci of infective inflammation—without any further reaction taking place than is necessary for the constitution of the reparative process. I need not remind you, gentlemen, that our London experience affords us examples (it is quite unnecessary for me to point out where they are to be found) that show that similar skill, care, and accuracy, even when not carried out on the principle of occlusion, lead to similar results; and, further, that in the past, on the whole, our hospital results, as is freely acknowledged by German surgeons, are far better than they have hitherto been on the other side of the Channel. But this consideration does not in the slightest degree detract from the value of German hospital experience for the scientific purposes we have now in view. When, as at Halle, we have pyæmic affections banished from wards which were formerly infested; when, as at Munich, hospital gangrene (a disease which probably a great many of us have never seen), which up to 1854 affected 80 per cent. of the traumatic cases in the hospital, has ceased to exist; when we see the same experience repeated at Strasburg, at Leipsic, at Innsbruck, and I know not at how many other places,—we need no longer wonder that it is common to hear the discovery of Lister spoken of in Germany as the greatest progress in the art of medicine which has taken place in modern times. But it is not, as I said before, with the human life saved and human suffering spared by his improvements that we have to do at present, but with the pathological lesson to be learnt from these results.

* "The individual particles of the finest floating matter of the air lie probably far beyond the reach of the microscope" (Professor Tyndall, *Philosophical Transactions*, 1876, Part 1, p. 44).

† "Der gefährlichste Staub ist derjenige von dem wir gar keine Wahrnehmung haben." Nägeli, *Die niederen Pilze in ihren Beziehungen zu den Infektionskrankheiten*. Munich, 1877, p. 153.

* It may be well to note that in Halle, as elsewhere in Germany, rapid improvement is in progress in all matters relating to medical education. Among other things, a magnificent surgical hospital is being built in the most airy part of the town, under Professor Volkmann's immediate direction.

The germ-theory explains everything by saying that the reason why a wound goes wrong is, that atmospheric particles enter in and contaminate it. It compares, in short, the treatment of an operation-wound with one of Professor Tyndall's or M. Pasteur's experiments on spontaneous generation. It professes, indeed, to be an application of the principles and method of such an experiment to a practical purpose. It is perfectly true that the same fastidious precautions which are necessary to command success in the one case are also necessary in the other. What, then, is the difference between them? In the laboratory experiment, the criterion of success is the absence of living organisms. If they appear in the test-liquid employed, the operation is considered as a failure; for, so far as experience has yet taught us, there is no case in which organisms come into existence otherwise than as the progeny or offspring of previously existing bacteria. Are we justified in applying the same test to the antiseptic treatment of an injured surface? From the theoretical point of view, we certainly are; for, on a wounded surface protected by antiseptic dressings, bacteria were to appear, then one of two things would be certain: either that the germs had entered from outside, or that they existed in the patient's organism previously. But is this the true criterion? Certainly not. In judging of the value of a therapeutical method, the one and only criterion is success. The question of primary importance is not whether bacterial germs are killed or sterilised, but whether the pathological results of septic infection are prevented, so that the wound is free from inflammation, the constitution free from fever. Consequently, whatever doubts we may be led to entertain as to the theory, those doubts ought not to interfere with our cordial acceptance of the evidence which has now been accumulated of its prophylactic value.

Some of you are probably aware that two series of observations have lately been published in Germany which go to show that, although in many instances the occlusive treatment is successful, not merely in warding off infective results, but also in the shutting out of germs, there are others in which the first object is completely accomplished—the patient remaining free from fever, pain, and inflammation—but yet organisms exist in the discharges. Obviously we might, if we chose, say, "Professor Lücke is not Professor Lister. It does not follow that, because organisms are found in the discharges from drainage-tubes at Strasburg, they should also be found at King's College." This, of course, may be freely admitted, but does not answer the objection. What is alleged is, that in these cases, although the method was carried out sufficiently perfectly to accomplish its end (the absence of pain, fever, inflammation), nevertheless organisms had found their way into the discharges; but that here, as elsewhere, being placed under conditions hostile to their development, they had been harmless.

If this be true, the inference to be drawn from it is, of course, that the treatment of a wound is not an experiment on spontaneous generation, but an experiment on infection: to use Professor Tyndall's striking expression, a combat not with atmospheric germs, but with pathological infectivity. Clearly, if it were purely a question of the exclusion of germs, the entrance of one germ would be fatal. But are there not hundreds of instances in which traumatic surfaces are exposed to germs without any effect whatever? Look at the ordinary results of the thousands of operations that are daily performed on animals for economical purposes without any precautions against germs. How often does infection occur? Not once in ten thousand times. Again, how often does it happen that an ordinary incised wound, notwithstanding that the knife that made it is beset with germs of many sorts, fails to heal straight off *per primam*? Again, in vaccination and in subcutaneous injection, do we not take every pains to do the operation in such a way as to promote absorption of whatever is on the surface of the instrument; yet who ever thinks of air-germs in connection with either of these operations? Dangers from infection, alas! attend both; but the infections we have to fear are of *pathological*, not *meteorological*, origin.

Now, these facts cannot be explained on the ground that the wounds in question are too inconsiderable; for we know by experience that, when real infection is in question, it is precisely by such wounds that it enters. For example, you will find, if you examine the records of outbreaks of hospital gangrene, that the wounds attacked were not suppurating or granulating wounds, but mere scratches or pricks.

I am desirous, in all that I say on this subject, to keep strictly within the limits of my own scope; I do not desire to make practical applications. My aim is to show that the principles which underlie the success of the antiseptic treatment are deeper than the surface of the wound. Let me, in conclusion, endeavour to indicate what those principles must be. The first principle that suggests itself on pathological grounds relates to the avoidance of conditions in the wound itself which favour the development of infectivity. Considering that the development of

infective action in a wound (supposing it to depend on the evolution of successive generations of organisms) must be a question of time, and that the circulating blood and living tissue are the most powerful colytics that we know in restraining and preventing that development, all methods which tend to prevent the accumulation of blood or liquids in wounds must be of great importance, not because these materials are in themselves incapable of being absorbed or organised, but because, if accumulated in quantities, they are withdrawn from the colytic influence of the living tissues.

The second principle I take to be the avoidance of infective contamination, in connection with which the question at once arises of the source of such contamination. If it be not atmospheric particles, what is it? Bear in mind that, wherever bacteria have been vegetating for some time in moisture containing the material for their growth (and we have seen how simple their requirements are in this respect), there infective virus is being elaborated. Consequently, that ordinary filth (of which the only scientific definition is, that it consists of the products of bacterial evolution) is more or less virulent or infective according to its development. Hence, if against all filth there lie a *prima facie* presumption that it is infective and a source of danger, scrupulous cleanliness must be essential. I need not add that, in antiseptic surgery and in the practice of those surgeons who have accomplished the greatest successes in the combat with traumatic infection, this principle is so well recognised that, in the future, we may hope to speak of "surgically pure" instruments as familiarly, and with as much significance, as we now speak of "chemically pure" substances. As may have been observed before, the colytic treatment is an importation of the methods and principles of the laboratory into the surgical ward.

But there is a third principle, which must not be forgotten. If there be any truth in what I have been saying as to the mode of origin of infective virus, the use of disinfectants, and among disinfectants of those which are known by experiment to be the most efficient colytics, must be of the greatest value. The benefits already derived from the use of carbolic acid are matter of accumulated clinical experience, and, as I have already hinted, even better results may be hoped for from other bodies belonging to the same category.

I have occupied so much time with the discussion of the origin of common, or traumatic, or phlogistic infectivity, that I have too little left for the other question I have to bring before you; namely, that of the intervention of living organisms—microphytes—in specific infection, *i.e.*, in the communication of specific diseases from diseased to healthy individuals, and in the development of the pathological consequences of such communication. This question, let me observe, although quite as important as the other, is so entirely unconnected with it, that no conclusions we have arrived at with respect to the origin of traumatic infection can be applied without reconsideration to that of *contagium vivum*. The septic poison we have seen to be an exclusive product of bacterial development, a product which bacteria are capable of manufacturing from unorganised and perfectly harmless material, a product which, although incapable of passing through certain kinds of filters, is soluble in the ordinary sense. Pathologically, we have seen that it does not act the part of a specific contagium; that, in order to the production of its morbid effects, a sufficient quantity must be introduced into the circulation; and, further, that the intensity of effect is proportionate to the quantity introduced; so that, if the amount be not too great, the tendency is to a favourable, not to a fatal, termination. But everyone knows that there occur from time to time in clinical experience instances of a sort of septicæmia of a much more virulent kind; cases, for example, of septic peritonitis, in which the quantity of the agent required to produce the fatal result is not measured by drops or grains, but (if one may so express oneself) in homœopathic doses; cases in which we at once recognise that we have to do, not with a poison of which the effect is determined by its quantity, but with a ferment of which the destructiveness to life is chiefly dependent on the rapidity of its development.

The history of these most malignant forms of septicæmia (I call it so for want of a better word) is simple enough. The gateway by which the seed enters may be, and usually is, a mere prick, and the primary effect so slight as to excite no attention. After hours, or even days, the absorbents and lymphatic glands, of which they are the tributaries, become the seat of inflammation, on which follows diffuse suppurative infiltration of the surrounding cellular tissue. Soon the process extends beyond the limb affected, to the integuments of the trunk, to the pleura, to the peritonæum; the inevitably fatal result, which is preceded by delirium and collapse, being partly, perhaps, due to the direct influence of the specific contagium, but principally to the enormous development in the organism of the ordinary septic poison.

These appalling cases must be clearly distinguished as regards their pathological nature from ordinary septicaemia. That they also have their mycological interpretation I have endeavoured to show by experiment. I have shown,* as regards peritonitis, that if the exudation of a simple peritonitis be injected fresh into the peritoneum of another animal, the disease assumes a more intense form in the second than in the first; that if in this way the disease be communicated to several animals, the effects will differ in different cases; that if by artificial selection the most severe case be picked out and the exudation from that case be used for further transmission, a still more intense inflammation will be the result, until at last a virus is obtained of which the virulence resembles that of the specific cases of malignant peritonitis in the human subject to which I have been referring. To account for the production of such cases, you have only to substitute accidental for intentional selection, the most important point to bear in mind being that the process by which the poison is developed, whether accompanied by a specific organic form or not, is a pathological process, that is, a process which can only go on in the living tissue, and which is necessarily associated with a certain definite succession of structural and physiological changes in the affected part. To obtain information respecting these processes, we must have recourse to experimental pathology. For example, experiments like those to which I have referred, which show how, by a gradual evolution, we may rise from common traumatic infectivity to the intensified virulence of malignant septicaemia, teach us what we could not learn otherwise.

From these cases, in which the direct intervention of a morbid organism is merely a matter of inference, I pass to the consideration of the only instances in which we are, at the present moment, able to say with confidence that we know the relation between morphological and pathological development. When I last had the opportunity of addressing you on the subject of contagious diseases, I enumerated four such diseases as the only ones in respect of which we are able to assign any pathological meaning to the organic forms which present themselves in the diseased parts. With reference to three of these, namely, relapsing fever, diphtheria, and small-pox, some new facts have been brought to light during the last two or three years; but before I refer to them, I will bring before you the very remarkable discoveries relating to the origin and development of the fourth member of the group—the epizootic anthrax of cattle—which have been made during the last year by a pathologist with whom I have lately had the pleasure of making acquaintance, Dr. Koch of Wollstein, in North Germany.

In my former lectures, and more fully in a paper which has been published in the *Reports of the Medical Officer of the Privy Council*, I gave an account of this remarkable disease, which I then called by the English name splenic fever. A still fuller description of the disease is now in the hands of English readers in Professor Bollinger's article in Ziemssen's *Cyclopaedia*. It is a disease of great rapidity, of which the prominent symptoms strikingly resemble those of septicaemia. Excepting in very rapid cases, which are often spoken of as apoplectic, a previous febrile stage may be distinguished, but in bovine animals death is preceded by alvine discharge and gradual loss of temperature. After death, the pathological appearances somewhat resemble those of septicaemia, in so far that capillary hæmorrhages occur in the affected parts, and that there are signs of disintegration of the blood-corpuscles and that the blood fails to coagulate after death; but there is this difference, that the disease exhibits special localisation, in some cases in the subcutaneous cellular tissue, in others in the submucous tissue, the change consisting in abundant discharge from the vessels of liquor sanguinis and of corpuscles. The existence of these infiltrations and the fact that the spleen is always intensely congested and swollen, constitute the naked-eye pathological characteristics of splenic fever. The facts which were known in 1874 relating to the propagation and essential pathology of splenic fever are fully stated in my paper.† Let me enumerate them: 1. The blood of a diseased animal communicates the disease by minimal inoculation to a healthy animal; 2. Such blood always contains, when in some stage of the disease, certain characteristic organisms—the so called bacilli of anthrax; 3. Blood which has been filtered through porcelain is not poisonous; 4. Blood taken from animal's in the acute stage cannot be kept for more than a week without losing its activity; 5. Notwithstanding this, there is evidence that in certain forms the poison is very persistent.

I suggested that this last fact could be explained by supposing that the organism (for here I may state by anticipation that I then regarded it, and still regard it, as completely made out that the specific pathological process is inseparably associated with the organism) that the organism is capable of existing in two states similar to those which we

know to exist in other cases, in one of which it undergoes rapid development but is of labile molecular structure; in the other, it is permanent and resistant.

My friend Dr. W. Roberts has complimented me on having anticipated the results of the investigations of this year. I cannot claim any special credit for this, for the indications afforded by the facts were too plain to be mistaken, so that I could scarcely fail to be right in my inference, if I paid sufficient attention. Knowing what I knew of the life-history of the group of organisms in question, it was not difficult to anticipate that, if such an organism existed, it must behave in the way suggested. Its development must be made up of an alternation of labile and stable states of existence—lability corresponding with rapid vegetation, stability with the apparent suspension of all those changes of the vital process which constitute life. The credit in such cases is due, not to the man who imagines how the thing is likely to happen, but entirely to the man who demonstrates what does happen by experiment or clinical observation. In this case, we must give it entirely and exclusively to Dr. Koch, who has proved experimentally that the blood of animals affected with splenic fever in its most acute form loses its activity very rapidly, but that certain kinds of blood may be kept for long periods, *e. g.*, of years. The contagious material must, therefore, exist in the blood in two forms. Blood which possesses the power of resisting contains, he says, not only the peculiar motionless sticks which are found in the blood and particularly in the enlarged spleen, of every diseased animal, but also certain oval glistening bodies which, from their mode of origin, Koch is justified in calling spores. The way in which the proof is given that they are so is the following. If you take the blood of an animal in the acute stage of the disease and cultivate it in serum at the temperature of the body, the organism begins at once to vegetate rapidly.* This growth does not, however, consist in multiplying of the sticks by division; for, on the contrary, the sticks prolong themselves into filaments of great length in which no divisions can be distinguished. Next a change takes place in the structure of the internal substance of each of these filaments, by virtue of which the protoplasm collects itself at certain points into masses. As time advances, these masses become more and more distinct, assuming finally the form of round or ovoid spores. Eventually, the filament fades away and the spores are liberated.†

Fig. 1.

Fig. 2.

Fig. 1.—Bacilli, as seen in a fresh preparation of an animal affected with splenic fever. The blood-corpuscles and bacilli are deeply stained by an aniline solution, which has been added for the purpose.

Fig. 2.—Felt-work of long unjointed filaments, into which the rods grow when transferred to humor aqueus, and kept at a temperature of 32 deg. C.

Fig. 3.

Fig. 4.

Fig. 3.—The same filaments twelve to twenty-four hours later. The formation of 'spores' in their interior has already commenced.

Fig. 4.—The spores in their complete stage. Some are free, but the most are still held together by the scarcely distinguished remainder of the filaments. The infecting power of these spores has been recently tested in the course of experiments now in progress.

* Dr. Ewart, of University College, has during the last few weeks been engaged in studying the development of the bacillus, and has been able to add very considerably to the facts relating to its development. The summary I give in my lecture is founded on the observations in which I had the opportunity of taking part, through the kindness of Professor Cohn and of Dr. Koch, in the laboratory at Breslau. I will not anticipate Dr. Ewart's results, which will, no doubt, be soon published. It is sufficient to say that they are of such a nature as to fix the morphological specificity of the anthrax plant with even more certainty than before.

† The figures have been copied from Dr. Koch's photographs, published in Professor Cohn's *Beiträge* since the lecture was delivered. They will serve to render the statements I have given more intelligible.

* *Medizinische Jahrbücher*, vol. vi, p. 417; and *Journal de l'Anat. et de la Physiologie*, July 1876.

† *Reports of the Medical Officer of the Privy Council*, new series, No. 8, p. 36.

It is these spores which contain the element of resistance. I shall be able at our next meeting to show you preparations illustrative of their development. Since the publication of Dr. Koch's paper, they have been studied by M. Pasteur, who states that they are not only resistant to putrefaction, but also to the boiling temperature and to the action of oxygen under high pressure.* M. Pasteur further states that he has cultivated them in urine for very long periods, and has found that they retain their virulence after repeated cultivation. In a pathological point of view, the importance of the whole research lies simply in this: that to a liquid, which is in itself harmless, viz., serum or aqueous humour, properties can be communicated by setting up in it a process of vegetation, of which the effect is that a virus is produced—a virus which has no relation to that of putrefaction, and acts in a specific—that is, peculiar, way; its action being to multiply with extraordinary activity in the blood and tissues of the living animal, and by virtue of such multiplication to destroy life.

I am anxious to place before you the facts which we possess in relation to splenic fever in the strongest light, in order that it may be clearly seen that the conclusion we are compelled by these facts to arrive at, in respect to this disease, is based on evidence of an entirely different nature from that on which the general theory of *contagium vivum* is supported. If I come forward and assert, as a matter of scientific observation in respect of any substance, whether a chemical body or an organism, that it is a virulent contagium, you have a right to require of me to prove it, not by referring to analogies or to the condition of its origin, but by experiment. And in this experimental proof two things must be included: first, I must show you that if I introduce it into the organism of a living animal in minimal quantity, it will sooner or later become the focus of a pathological process; and secondly, I must prove to you that the virulent substance which thus acts in producing the specific disease, is itself a product of that disease, that is, that it can be obtained directly from the body of the diseased animal. It is on this ground that we proceed whenever we rightly apply the term contagium. Thus, in the case of vaccine, we correctly apply the term to vaccine lymph, because, on the one hand, it is a product of the process of vesication; and, on the other, produces with certainty a vesicle. In a word, it is at the same time a seed and the fruit of the disease. As regards cow-pox, therefore, we have the most complete certainty as to the existence of a contagium, and have it, as it were, between thumb and finger. Of its nature we know nothing as yet, excepting that it is particulate. As regards the question whether these particles possess organic structure or not, in other words, whether they possess the power of vegetative development which is associated with their morbid action, we know absolutely nothing. That organisms are present is certain enough, and that they are peculiar, but of their function nothing has as yet been ascertained. Mr. Godlee's experiments, which, as regards skill and accuracy, left nothing to be desired, go to show that the organisms which are always found in the liquid fail to afford evidence of their pathogenic properties. The same remarks apply to the organism of small-pox. Another similar example is that of diphtheria. It is perfectly certain that, in every case of faucial diphtheria, a mycotic process goes on in the affected mucous membrane; in other words, that the vegetation of micrococci is an element in the peculiar inflammation which gives rise to the diphtheritic concretion. And inasmuch as, from clinical observation as well as experiment, we know that the concretions contain in themselves the specific contagium, it is impossible to dispute that in every case in which the disease is communicated by contagium, that communication may take place through the organisms, but the proof is as yet entirely wanting.

With reference to both diseases, I mean both to small-pox and diphtheria, we have evidence of another kind, which is of great importance. Although the two have little resemblance, they correspond with each other in this respect, that both are followed by secondary affections in internal organs—that in both it is the same organs which suffer, viz., lungs, liver, kidneys, and heart. As regards diphtheria, an excellent description of them, founded on cases, has been given by a French writer, M. Labadie-Lagrave,† but without histological details. The most remarkable of these lesions, and the one which is of most interest in relation to our present inquiry, is the valvular endocarditis, which, according to M. Lagrave, occurred in more than half of the forty-six fatal cases under his observation. Now, this affection, of which, as a complication of diphtheria, he has given a good account, is the same as the "ulcerative endocarditis," which was described, perhaps for the

first time, by Dr. Kirkes, and has subsequently been noted by others in various infective diseases, particularly Dr. Moxon,* by the late Dr. Fuller in erysipelas, by Dr. Dickinson in pyæmia, by Trousseau, and, if I am not mistaken, by Dr. West in scarlatina, by Wunderlich in measles; and has been recently more completely studied by Dr. Heiberg‡ in puerperal pyæmia, and by Dr. Weigert in small-pox.¶ Now, in all these cases the endocarditis has a doubly infective character. It is itself the consequence of an infection, and the focus from which infection spreads; for it appears to be closely associated with affections of the kidneys, liver, and lung, which exhibit such characters as might well be accounted for by supposing that minute portions of infective material had become free from the diseased valves, carried away by the blood-stream, and thus disseminated in the affected tissues. The endocarditis presents itself in two stages. The early stage, in which what is seen is that the edge of the valve (usually, but not always, the mitral) is beset with a little chain of greyish miliary elevations on a redder ground; and a later stage, in which a process resembling ulceration has occurred, in which evidently the material forming the nodules has disintegrated.

The whole subject of infective valvular endocarditis and its concomitant disseminated affection of other organs requires a great deal of study, and I do not know any subject at the present moment more worthy of clinical and pathological investigation. But the point that I have now to bring under your notice is that, in the only diseases in which the lesions have been investigated anatomically, pyæmia and small-pox—in the former by Heiberg, in the latter by Weigert—it has been found that the affection of the valves is mycotic, that is, that the thickening of the endocardium which takes place—a thickening which has its seat in the intima—is associated with the development of colonies of micrococci; and, further, that the punctiform foci of dead-alive material which occur in other organs are not minute abscesses, not foci of inflammation, but spots where localised tissue-death has occurred in consequence of little masses of the same kind which have either migrated from the affected valves, or quite as probably have found their way from the lymphatics of the affected skin—those vessels being in the early stages of malignant small-pox to a greater or less extent, occupied, as Dr. Klein and Dr. Weigert have shown, with the same organisms. In its bearings on the notions we must entertain as to the action of micrococci in the organism, these disseminated foci are of great interest and importance, for they show two things very plainly, viz., first, that, although ordinary bacteria cannot live in the circulating blood, yet there are organisms allied to these which can live and thrive after their own slow way—organisms which do not exhibit either the miraculous prolificness or the active motions of septic bacteria, but grow together in colonies of motionless spheroids; and secondly, that, when such organisms are present, they produce very little irritation in the tissues with which they are in contact.

The observations of Weigert show conclusively that the effect of the dissemination of these masses is not to produce foci of inflammation, but simply of necrosis. In the first instance, whenever the opportunity offers itself of investigating the lesions in its earliest stage, it can be made out with respect to each mass of micrococci—1. That it is enclosed in a vascular cavity; and 2. That it is surrounded by a zone of altered tissue, within and around which, although the elements have undergone a peculiar kind of degeneration, there are not any inflammatory changes. Eventually this island of altered tissue becomes the seat of cellular infiltration, and you have before you what may be termed a miliary abscess, but even then it is still possible to demonstrate in the centre of each such abscess the original mycotic nucleus.

What do we learn from this? 1. That, in certain infective diseases, of which erysipelas, diphtheria, and small-pox may serve as examples, the preliminary local processes which constitute the essential feature of the local lesions, whether primary or secondary, are associated with, and in great measure consist of, the development either in lymphatics or in blood-vessels of micrococci. 2. That these organisms have little or no resemblance to the bacteria or septic processes, being distinguished from them by their form, but chiefly by their mode of growth, that is, by the circumstance that they grow in rounded masses or colonies. Although obviously connected in their development with infective processes, they do not in the slightest degree resemble the infective organism of splenic fever. They show no tendency to multiply in the cir-

* See Dr. Moxon's "Case of Ulcerative Endocarditis of the Right Heart", *Pathological Transactions*, vol. xxi, 1870, p. 107.

† Heiberg, "Ein Fall von Endocarditis ulcerosa puerp.", (Virchow's *Archiv*, vol. lvi, p. 407). See also a case recorded by Gerber and Birch-Hirschfeld in the *Arch. der Heilk.*, vol. xvii, p. 208; another by R. Maier, in Virchow's *Archiv*, 1874, vol. lxiii, p. 145; and an important paper by Virchow himself on Puerperal Endocarditis, in the *Beiträge zur Gynäkologie*, 1872.

‡ See Weigert, *Anatomische Beiträge zur Lehre von den Pocken*, Part ii; Breslau, 1875.

* Pasteur, *Charbon et Septicémie*, Paris, 1877, pp. 10 and 11. M. Pasteur declares that whereas the filaments perish at once in oxygen under a pressure of ten or twelve atmospheres, the spores, or, as he calls them, "corpuscules germes", are unaffected, and that blood containing them, when so treated, retains its virulence.

† *Les complications cardiaques du Croup et de la Diphthérie, et en particulier de l'endocardite secondaire diphthérique*, par le Dr. Labadie-Lagrave. Paris: 1874.

culating blood, nor, indeed, to spread their influence at all beyond the tissues in which they have taken up their residence.* They are associated in every instance with local, not with general, processes—with processes which spread by continuity of tissue, not with general infection of the whole organism. What the nature of that relation is, I still think, as I thought when I last had occasion to speak on this subject, must remain open. The view which commends itself to my mind as by far the most probable, is that, whatever may be the original nature of the primary disease in association with which they present themselves, the organisms are specifically the same; that they reciprocally are modified by, and modify the soil in which they find themselves, and, by virtue of this interaction, take as important a part in the secondary processes to which they belong as pus-corpuscles take in the process of inflammation. Whether they are in any respect entitled to be regarded as specific contagium particles, whether they possess the power either of conveying the contagium from a diseased part of the organism to a healthy, or from one diseased body to another, we are still bound, I repeat, to regard as an open question.

CLINICAL LECTURE ON PHLEBITIS.

By WILLIAM S. SAVORY, F.R.S.,
Surgeon to St. Bartholomew's Hospital.†

THE phenomena of phlebitis—its symptoms—are comparatively simple, and for the most part sufficiently clear. The disease often starts with pain—or, perhaps, more accurately speaking, aching—and acute tenderness in the course of the affected vein, which in the majority of instances, I think, at the outset presents to the touch evidence of being plugged. At other times, beyond perhaps an aching of the leg or other part, the only local evidence of the mischief is oedema. But this is usually, I think, very significant. The oedema of this affection is firmer, and apparently more generally diffused throughout the limb, than when it is due to simple obstruction or failure of the circulation. The affected limb, or part of it, is enlarged and thickened, but often with comparatively little alteration of shape, the skin pale and tense, and, when the part is grasped, the texture feels uniform and solid. One misses the characteristic pitting, upon moderate pressure, of ordinary oedema. The whole condition of the limb seems one rather of the state in which it is often left after an attack of phlegmonous erysipelas. And it seems to me important to distinguish between these two classes of cases: those which commence with local pain and tenderness, and those which are marked only by oedema; for, in the former case, the superficial veins only are at fault; in the latter, the deeper veins.

Take this case. Ernest C., aged 26, a barman, of dark complexion, well built, although inclined to be fat, and strong, was admitted into the hospital in the following condition. The right foot, leg, and thigh are much enlarged by firm oedema. The right thigh in the middle measures $23\frac{1}{2}$ inches, the left $20\frac{1}{4}$ inches. The skin is very tense and somewhat injected, and above the right ankle in the lower half of the leg it is eczematous. This part, he says, was the seat of an ulcer two years ago. In the upper part of Scarpa's triangle, in the position of the femoral vein, a hard and tender cord can be felt on deep pressure. There is also slight tenderness over the iliac fossa. The epigastric veins are conspicuous. He told us that, nearly two years ago, after a long boat-race, he noticed that the veins of the right thigh were prominent. Three or four months later, he found one day, after hard work, that the right ankle was swollen, but on the following morning this had subsided. From that time, however, the foot and ankle were often enlarged, and the swelling gradually extended upwards, so that for the last year the leg, knee, and lower part of the thigh were markedly larger than on the left side. His health was not affected until just previously to his admission, when he began to suffer pain along the course of the femoral vessels, and then the whole of the right limb became much swollen and very tense. He admitted that he had drunk freely of beer, and had syphilis six years ago. For some days after his admission, the pain disturbed his rest. His temperature rose from 101.8 deg. to 103.6 deg. The swelling of the thigh increased until it measured at the middle 25 inches. On the fourth day after admission, he had four attacks of epistaxis and one was copious. His temperature fell, and the next day it was normal. During the following week, the swelling

of the thigh subsided, until, at the expiration of a fortnight from his admission, there was very little difference in the size of the two limbs. But, for a week or two longer, a hard cord could be distinctly traced through Scarpa's triangle. He was kept in bed with the limb still. Strong lead lotion was applied at first, and afterwards a flannel bandage.

I may, perhaps, be allowed to publish the following note, which I made when I worked in the out-patient room of the hospital. I have seen, within the last twelve or fifteen months, eight or ten cases of this description. A person previously in tolerably good health, or at all events having no definite cause of complaint, is rather suddenly seized, without any obvious reason, with diffused pain in the calf of the leg. The pain, which is usually severe, is soon followed by a sense of extreme tension and by swelling, which, for a few hours or a day or two, gradually increases. When the leg is examined, the whole of it below the knee to the ankle is considerably swollen, tense, and very tender about the calf. In some cases, the induration is very marked. The surface will hardly yield to firm pressure. There is no elasticity, but a sense of hardness, as if something had been effused into the cellular tissue which had set and rendered the whole solid. By-and-bye, or in some cases from the first, the hardness is more circumscribed, and limited to the calf. There is never at first, and often not throughout, any discoloration of the surface. It is usually pale, tense, and somewhat shining. In favourable cases, the whole will gradually, almost imperceptibly, subside, and the limb resume its natural condition. In others, a sense of fluctuation gradually arises in the thickened and indurated calf, and this is followed by a blush on the surface. An incision, in these circumstances, will let out a considerable quantity of well-formed, but usually more or less blood-stained, pus.

With all this, a careful examination will in most cases fail to discover any morbid or unnatural condition of the veins of the limb. The femoral and superficial veins will appear natural. In some cases, however, the femoral vein is obviously thickened and tender, and can be traced as a cord through a portion of the thigh. There is usually little or no constitutional disturbance. Where the opportunity has been given, of course, the patients have been kept at rest; but, in more than one instance, they have continued to attend at the out-patient room, even walking to and fro, yet all has gone on well—in these cases it has happened without suppuration—and the limb has been restored.

Now, what is the pathology of these cases? Looking at their history and the features they present, I regard the veins as the primary seat of mischief. That the femoral vein itself is involved in some of the cases, is a matter of certainty. And those cases in which all the veins in reach of the senses appear normal, so closely resemble the others in which the veins are obviously at fault, that it is impossible not to refer them to one and the same pathological cause. If any opportunity of dissection were afforded me, I should expect in these last cases to discover something wrong in the deepest veins. I will not venture at present, on such slender evidence, to speculate further on the pathology of these most interesting cases. It is difficult to explain all the changes that ensue by simple venous obstruction, even though that were general; and, assuming this to exist, I could only guess at the cause of it. The cases are striking ones, and form a distinct class. That their pathology involves some change in the veins, I strongly believe. Beyond this, I dare not go.

Again, when the veins affected can be traced, the extension or course of the disease may be observed in two forms. There may be a simple extension, either gradual or rapid, of the pain, tenderness, solidification, and distension in the course of the affected veins; or these local signs may exhibit a striking want of uniformity. They may shift from vessel to vessel, or from one portion of a vessel to another, and in this way wander irregularly over the surface of the limb; subsiding in one part and starting afresh in another; fluctuating from week to week, or even perhaps from day to day, but withal obstinately inclined to linger, and to disappoint us of expected convalescence. Paget says of gouty phlebitis: "In such cases, the phlebitis may have no intrinsic characters by which to distinguish it; yet, not rarely, it has peculiar marks, especially in its symmetry, apparent metastases, and frequent recurrences." (*St. Bartholomew's Hospital Reports*, vol. ii, page 83.)

Here is an instance. E. C., about 50, was a stout, heavy muscular man, abstemious, very active, and in apparently good health. He had suffered, however, two or three times from "rheumatism in the knees and legs", once rather severely, for which he sought relief from the mud-baths of Marienbad, which "always cured" him. In both legs, below the knees, the veins were somewhat varicose. He came complaining of pain in one leg, and there was an oval dusky patch, brawny to the touch, as large as the palm on the inside in the middle third. The tortuous internal saphena vein was very tender, somewhat thickened, and here and there apparently solid; but, in the midst of the thickened tissues, it could hardly be defined. This continued to trouble

* In this and the preceding statements relating to small-pox, I have followed Dr. Weigert, who was good enough to show me his preparations when I was in Breslau last October.

† Concluded from page 149 of last number.