October 1874, the best appointed medical school in the provinces was opened. The advantages of the union have not only accrued to the Medical School, by providing increased accommodation and greater facilities for experimental medicine, but also to the College, in thus rapidly increasing its numbers, and adding to its area of usefulness.

The infirmary authorities are now invited to take their share in furthering the cause of Scientific Medical Education; to do this effectively, the disadvantages under which we have so long laboured from having a defective hospital must be remedied.

It is unnecessary that I should occupy more of your time when there is so much that is interesting to be brought before you during the meeting of our Association.

I have dwelt at length on the subject of hospitals and their connection with medical education, holding, as I do and have long done, the deep conviction that it is a question of the highest importance in all its bearings, and this not only to medical men, but to every member of the community. I believe I shall have the sympathy of this great and influential meeting in the views I have expressed and in the statements I have made.

Allow me in conclusion, gentlemen, to offer you once more our sincere welcome to Manchester.

ADDRESS IN MEDICINE,

BY

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Physician to the Manchester Royal Infirmary; Professor of Clinical Medicine in Owens College; etc.

THE DOCTRINE OF CONTAGIUM VIVUM AND ITS APPLICATIONS TO MEDICINE.

GENTLEMEN,—The notion that contagious diseases are produced by minute organisms has prevailed in a vague way from a remote age; but it is only within the last twenty years—since the publication of Pasteur's researches on fermentation and putrefaction—that it has assumed the position of a serious pathological doctrine. In the last decade, startling discoveries of organisms in the blood have given this doctrine the support of actual observation; and its application as a guide in the treatment of wounds by Professor Lister has made it a subject of universal interest to medical practitioners.

The resemblance between a contagious fever and the action of yeast in fermentation—or the action of bacteria in decomposition—is in many points so striking that it is difficult to avoid the impression that there is some real analogy between them. If, for example, we compare the action of yeast with small-pox, this resemblance comes out very distinctly, as the following experiment will show. I filled two pint bottles, A and B, with fresh saccharine urine, and inserted a delicate thermometer in each. A was inoculated with a minute quantity of yeast, but nothing was added to B. Both bottles were then placed in a warm place in my room, at a temperature of about 70 deg. Fahr. In order to get a correct standard of temperature for comparison, I placed beside these a third bottle, C, filled with water, and inserted a delicate thermometer in it. All these bottles were carefully swathed in cotton-wadding, for the purpose of isolating their individual temperatures, and to obviate, as much as possible, the disturbing effects of the varying temperature of the room. For twelve hours no change took place; but, at the end of this time, A began to ferment, and the thermometer marked a distinct elevation of temperature. On the second day, A was in full fermentation, and its temperature was 2.7 deg. above B and C. This disturbance continued for five days, the temperature ranging from two to three degrees above the companion bottles. The disturbance then subsided, and the temperature fell to an equality with B and C, and a considerable sediment, composed of yeast, settled at the bottom. In the meanwhile, B showed little alteration; but, on the sixth day, it began to ferment, the temperature went up, and for more than a week its thermometer stood about two degrees above A and C. Finally, the temperature in B declined, the disturbance subsided, and the newly formed yeast settled to the bottom of the vessel.

This fever in a bottle resembled small-pox in the following points.

A period of incubation intervened between inoculation and the commencement of disturbance; then followed a period of disturbance accompanied by elevation of temperature; this was succeeded by a subsidence of the disturbance and a return to the normal state. Great multiplication of the infective material (or yeast) took place during the process, and, after its conclusion, the liquid was protected from further infection with the same contagium. We likewise notice that the contagium of fermentation, like that of small-pox, may take effect either by direct purposive inoculation or by fortuitous infection through the atmosphere. In both cases, the infective material has the power of preserving its activity for an indefinite period. The comparison fails in at least one important point—in the fermented urine, sugar is replaced by alcohol and carbonic acid; but we are not aware that any pronounced chemical changes occur in the blood or tissues during an attack of small-pox. I would, moreover, carefully guard myself against being supposed to suggest that the enhanced temperature in the fermenting urine is a real analogue of the preternatural heat of fever.

Let me direct your attention to another example—a kind of partial decomposition or fermentation which takes place in boiled hay-infusion when it is inoculated with the *Bacillus subtilis*. The *Bacillus subtilis* is a very common bacterium found in vegetable infusions and in curdling milk. I hope you will take note of this little organism; for I shall have to refer to it more than once in the course of this address. I took a flask containing hay-infusion, which had been sterilised by boiling, and inoculated it with a drop of fluid swarming with *Bacillus subtilis*. After the lapse of twenty-four hours, the previously transparent infusion became turbid. This turbidity increased, and, on the second day, a film or crust formed on the surface of the infusion. On the third and subsequent days, the crust broke up and fell in pieces to the bottom of the vessel. In about a fortnight, the turbidity passed away, and the original transparency of the infusion was perfectly restored, so that it looked exactly as it did before the process began, except that there was now a sediment consisting of the spores of the little organism at the bottom of the flask. In this case, again, there was the same succession of events: a period of incubation, followed by a period of disturbance, succeeded by a period of subsidence, and, finally, restoration to the normal state. There was also great increase of the infective material and immunity from further attack by the same contagium.

The yeast-plant and the *Bacillus subtilis* may be taken as representatives of a large class of organisms in regard to which we are only beginning to realise their vast importance in the economy of Nature and in the life of man. They are, as I shall presently show, the essential agents in all fermentations, decompositions, and putrefactions. We may group them together for the convenience of description under the general designation of *saprophytes*, a term intended to include under one heading all the organisms associated with the decomposition and decay of organic matter. The yeast plant and its allies, and all the numerous species and varieties of bacteria, belong to this group. In size and form, they are among the smallest and simplest of living things, but their vital endowments are wonderful.

All the organisms hitherto found associated with infective inflammations and contagious fevers belong to the tribe of bacteria, and we cannot advantageously enter on a study of that association without a knowledge of the origin and attributes of these organisms. This brings us into a field of active controversy. It has been alleged, as you know, on high authority, that these organisms, under certain conditions, depart entirely from the universal law of generation, which is expressed in the aphorism *omne vivum ex vivo*, and that they may arise spontaneously by a process of abiogenesis. It is also alleged that these organisms are not the actual agents of decomposition, but are merely associated with that process as secondary or accidental accompaniments. I propose to lay before you evidence that both these allegations are unsustainable, and to prove that bacteria, like other organisms, arise from pre-existing parent germs, and in no other way, and that they are the actual agents in all decomposition and putrefaction.

The first proposition I shall endeavour to establish is this: that organic matter has no inherent power of generating bacteria, and no inherent power of passing into decomposition.

I have here placed before you samples of three sets of preparations, out of a large number in my possession, which serve to substantiate this proposition.

The first set consists of organic liquids and mixtures which have been rendered sterile by a sufficiently prolonged application of the heat of boiling water. They are composed of infusions of vegetable and animal substances, fragments of meat, fish, albumen, and vegetables floating in water. They are contained in oblong glass bulbs, and are protected from the dust of the air by a plug of cotton-wool inserted into the necks of the bulbs, but freely open to its gaseous elements

which pass in and out through the cotton-wool. They are all, as you see, perfectly transparent and unchanged, though most of them have been in my possession for several years.

The second set consists of organic liquids which have been simply filtered under pressure through unglazed earthenware into sterilised flasks. They include acid and neutralised urine, albuminous urine, diluted blood, infusions of meat and of hay. As these preparations were obtained by a method which is in some respects new, I will describe it to you. A piece of common tobacco-pipe, about six inches long, served as the filter. This was secured by India-rubber piping to the exit-tube of one of the little flasks used by chemists for fractional distillation. The flask is first charged with distilled water, and then a tight plug of cotton-wool is inserted into its neck. The flask is next set a-boiling briskly over a lamp. The steam rushes through the cotton-wool plug and through the tobacco-pipe, clearing both these passages of any germs they might contain. When the water has nearly boiled away, the end of the tobacco-pipe is hermetically sealed with melted sealing-wax. After a little more boiling, the flame is withdrawn and the neck of the flask is instantly closed with a tight vulcanite cork. The apparatus is now ready for action, and the tobacco-pipe is immersed in the liquid to be filtered. When the flask cools, a vacuum is created within it, and this serves as a soliciting force to draw the liquid through the earthenware into the flask. The process of filtration is very slow; it takes two or three days to charge the flask. When a sufficiency has come over the apparatus is removed and placed on a shelf for a few days until the pressure inside and outside the flask is equalised. The vulcanite cork is then withdrawn, and the exit-tube is separated and sealed in the flame of a lamp. In this way, you obtain a sterilised flask charged with the filtered organic liquid, and protected from outside contamination by a plug of cotton-wool. Preparations obtained in this way, if due precaution have been used in the manipulation, remain permanently unchanged; organisms do not appear in them, and decomposition does not ensue.

The third set of preparations are in some respects the most significant of the three. They consist of organic liquids which have been simply removed from the interior of the living body, and transferred, without extraneous contamination, into purified glass vessels. I will not detain you with the methods employed to obtain them; it is sufficient to say that, by the use of proper precautions, it is possible to convey blood, pus, urine, ascitic fluid, pleuritic effusion, blister serum, or the contents of an egg into sterilised glass vessels without contact with any infecting agency. Preparations thus obtained are exhibited in these flasks; they are protected from air-dust by a simple covering of cotton-wool. All of them are absolutely free from organisms and from any signs of decomposition.

What meaning can we attach to these preparations? You all know that liquids and mixtures such as these speedily decompose and swarm with organisms when left to themselves exposed to the air. They are of most varied composition, and the most apt of all known substances to breed bacteria and to become decomposed. They have been exposed to the most favourable conditions in regard to warmth, moisture, and air. Many of them have been in my possession several years, and all of them for several months, yet they are wholly barren and without sign of decomposition. I venture to say that these preparations substantiate in a positive manner the proposition with which we started; namely, *that organic matter has no inherent power of generating bacteria and no inherent power of passing into decomposition.*

A second proposition is likewise established by these preparations; namely, *that bacteria are the actual agents of decomposition.*

In all the preparations, the absence of bacteria coincides with the absence of decomposition. If I were to cause bacteria to appear in them either by purposive infection or by exposing them to the unfiltered air, decomposition would infallibly follow. The filtration experiments supply a new and telling argument on this point. Some of the liquids became decomposed and full of bacteria while the filtration was going on, but the part which came over into the flasks remained without further change, showing that decomposition cannot go on without the actual contact of the living organisms.

We have next to ask ourselves what are the sources and what is the nature of the fecundating influence which causes organic liquids, when abandoned to themselves without protection, to become peopled with organisms. In regard to their source, the answer is not doubtful. If I remove the covering of cotton-wool from any of these preparations, and admit unfiltered air, or a few drops of any ordinary water, however pure, or anything that has been in contact with air or water, organisms make their appearance infallibly in a few hours. As to the nature of the infective agents, we can say positively that they must consist of solid particles, otherwise they could not be separated by filtration through cotton-wool and porous earthenware. Is it not a most natural

inference that they are the parent germs of the brood which springs up at their impact? They are, however, so minute that we cannot identify them as such under the microscope; but Professor Tyndall has demonstrated that air which is optically pure—that is, air which is free from particles—has no fecundating power.

It is contended in some quarters that these particles are not living germs of any sort, but simply particles of albuminoid matter in a state of change which, when they fall into an organic liquid, communicate to it their own molecular movement, like particles of a soluble ferment, and so produce decomposition which, in its turn, provides the conditions necessary for the abiogenic generation of bacteria. Filtration through porous earthenware furnishes a complete answer to this theory; for I found on trial that the soluble ferments passed with ease through the porous earthenware. If, therefore, this theory were true, the filtered liquids, if already commencing to be decomposed, would go on decomposing, and would develop bacteria after filtration; but instead of that they remain unchanged and barren. We are absolutely driven to the conclusion that these particles are living germs: no other hypothesis squares in the least degree with the facts of the case.

We may formulate this conclusion in a third proposition as follows: *The organisms which appear as if spontaneously in decomposing fluids owe their origin exclusively to parent germs derived from the surrounding media.*

But how, you will ask, has it been possible, in the face of this evidence, to maintain, with a show of success, the contrary opinion that bacteria can and do, exceptionally at least, and in certain media, arise spontaneously. This opinion is based on two undoubted facts, which, taken together, seem at first sight to stand in direct contradiction with the propositions I have enunciated. The first fact is that bacteria are invariably killed when exposed to a temperature of about 140 deg. F., or any higher temperature. The other fact is that certain liquids, such as neutralised hay-infusion and milk, often produce bacteria after having been boiled—sometimes after having been boiled for two or three hours—and when there was no possibility of subsequent infection. It seemed at first sight a fair inference from these two facts that the apparition of organisms in boiled liquids was due to spontaneous generation, or abiogenesis. It does seem difficult to believe that any living thing can survive a boiling heat for several hours—and yet such is undoubtedly the truth. When I published on this question in 1874, I advanced more than one line of proof which appeared conclusive that germinal particles of some sort did, under certain circumstances, survive a boiling heat; and that the instances referred to were examples of such survival, and not of a *de novo* generation. But I was not then able to explain the apparent contradiction involved in these experiments.

Since then, a new and surprising light has been thrown on this subject by the researches of Professor Cohn of Breslau, and we are now in a position to offer a complete solution of the riddle. All the confusion has arisen from our having failed to distinguish between the growing organism and its seed or spore. You are all familiar with the immense difference in vital endurance between the seed and the growing plant. The same difference exists between a spore and its offspring. Some spores have an extraordinary power of resisting heat. Mr. Dallinger and Dr. Drysdale, in the course of their inquiries into the life-history of septic monads, demonstrated that while the living monads are killed by a heat of 140 deg. F., the spores of one variety, which are so minute that they cannot be seen, except in mass, by the highest powers of the microscope, are capable of germinating after being subjected to a heat of 300 deg. F. for ten minutes! If the spores of monads can resist this tremendous heat, there is no reason why the spores of bacteria should not be able to survive the feebler heat of boiling water. The development of bacteria in hay-infusion, after having been boiled continuously for several hours in hermetically sealed vessels, seemed to furnish the very strongest attainable evidence in favour of the abiogenic origin of these organisms; and yet, by a singular fatality, the investigations of Cohn have shown that this evidence, rightly interpreted, supplies a crowning argument against that view.

Cohn had the curiosity to examine the organisms which arose under these extraordinary circumstances. Did he find a new birth? On the contrary, he recognised a familiar form: none other than our old acquaintance the *Bacillus subtilis*. He followed it through all the stages of its development. It first appeared some twenty-four hours after the boiling, in the form of innumerable short moving rods. On the second day, these rods shot out into long threads; on the third day, there appeared on the threads, at perfectly regular intervals, strongly refractive oval bodies, which he identified as spores. Finally, the threads broke down and the spores were set free. In many hundred observations, he saw this one organism and no other, and witnessed the successive stages of its development occurring with the constancy of a physical experiment.

Now, let me ask if this looks like an act of abiogenesis. The evolutionist demands, for the transformation of one organic type into its next descendant, myriads of generations, and I know not what lapse of ages. But here, if this be a case of abiogenesis, we see accomplished at one leap, in a single generation, and in seventy hours, not merely the bridging over of the gulf between the dead and the living, but the development of a specifically distinct organism, with definite form, dimensions, and mode of growth, and furnished with a complete provision for the reproduction of the species! I need scarcely say that such a feat would be, not only without parallel in the history of evolution, but would be wholly contradictory to that theory.

The only group of bacteria, so far as is known, which form spores are the *Bacilli*; and Cohn remarks that in all the various cases in which he had observed organisms to arise in boiled liquids, they belonged in every instance to the *Bacilli*.

Before leaving this part of my subject, I wish to suggest certain considerations in regard to the nutrition and function of saprophytes, which appear to me to render it in the highest degree improbable that spontaneous generation should ever be discovered in this quarter. If it be assumed that the occurrence of abiogenesis, at some time in the past history of the globe, is a necessary postulate in science, and I see nothing unscientific—looking to the law of continuity in the operations of nature—in the supposition, that it is occurring at the present day somewhere or other on the earth's surface, but certainly not in decomposing liquids.

Saprophytes are, as is well known, destitute of chlorophyll, and, like all such plants, they are unable to assimilate carbonic acid. They obtain their carbon exclusively from more complex compounds which have been prepared for them by pre-existing living beings. It is, therefore, manifestly impossible that the primordial forms of life could have belonged to this group; for if we throw ourselves back in imagination to that remote era when life first appeared on the globe, we should find ourselves in a purely inorganic world—amid conditions in which saprophytes could not possibly live nor obtain nourishment. The special function of saprophytes in the order of nature is to destroy, not to create, organic matter; and they constitute the last, not the first, link in the biological chain. For if we regard the order of life as it now proceeds on the earth's surface, we may describe it as beginning with the chlorophyll body, and ending with the saprophyte. The chlorophyll body is the only known form of protoplasm which obtains all its nutriment from inorganic sources: here integration is at its maximum, and disintegration at its minimum; and the resultant of the nutritive operations is increase of organic matter. The saprophyte, on the contrary, feeds on nutriment prepared for it by other beings: here integration is at its minimum, and disintegration at its maximum, and the resultant of the nutritive process is decrease of organic matter. What takes place in a decomposing liquid, under the action of saprophytes, is progressive disintegration, and finally a breaking up of all the organic compounds it contains into carbonic acid and ammonia; and the process ends with the mutual destruction of the organisms themselves. Organisms could not, therefore, begin in this way. The primordial protoplasm must have been either the chlorophyll body itself, or a body having a similar mode of nutrition.

If the search for contemporary abiogenesis is to be continued, as doubtless it must be, for science is insatiable, it appears to me that the inquirer should endeavour to realise the conditions under which abiogenesis must have occurred in the first instance. For, if the process be going on amongst us at this day, it may be assumed as probable that it still proceeds on the original lines laid down at the dawn of life. If ever I should be privileged to witness an abiogenic birth, I should certainly not expect to see a saprophyte: I should rather expect to see a speck of protoplasm slowly formed, without definite shape or dimensions, and nourishing itself, like the chlorophyll body, on a purely mineral diet. The more one reflects on this subject, the more clearly does it appear that the spontaneous origin of saprophytes is logically impossible. Speaking as an evolutionist, I should rather infer that saprophytes were a late development; probably a degradation from some algal forms which had found their profit in feeding on waste organic matter, and which gradually lost their chlorophyll through want of use, and with it their power of feeding on an exclusively mineral diet.

We now approach the more practical side of our subject: that which concerns us as practitioners of medicine and students of pathology. I have already directed your attention to the analogy between the action of an organised ferment and a contagious fever. The analogy is probably real, in so far at least that it leads us to the inference that contagium, like a ferment, is something that is alive. We know of nothing

in all our experience that exhibits the phenomena of growth and self-propagation except a thing possessed of life.

This living something can only be one of two things: either it is an independent organism (a parasite) multiplying within the body or on its surface, or it is a morbid cell or mass of protoplasm detached from the diseased body and engrafted on the healthy body. Possibly, both these conceptions may have their application in the explanation of different types of infective diseases. In regard to the latter conception, however—the graft theory—which has been so ably developed by my friend Dr. Ross, I will only say that it has not, as yet, emerged from the region of pure speculation. It lacks an established instance or prototype; and it fails to account for the long-enduring dormant vitality so characteristic of many contagia, which conforms so exactly with the persistent latent vitality of seeds or spores, but which contrasts strongly with the fugitive vitality of detached protoplasm.

If, then, the doctrine of a *contagium vivum* be true, we are almost forced to the conclusion that a *contagium* consists (at least in the immense majority of cases) of an independent organism or parasite, and it is in this sense alone that I shall consider the doctrine.

It is no part of my purpose, even if I had the time, to give an account of the present state of knowledge on this question in regard to every contagious disease. My object is to establish the doctrine as a true doctrine; to produce evidence that it is undoubtedly true in regard to some infective inflammations and some contagious fevers. In an argument of this kind, it is of capital importance to get hold of an authentic instance; because it is more than probable—looking to the general analogy between them—that all infective diseases conform in some fashion to one fundamental type. If septic bacteria are the cause of septicæmia—if the spirilla are the cause of relapsing fever—if the *Bacillus anthracis* is the cause of splenic fever—the inference is almost irresistible that other analogous organisms are the cause of other infective inflammations and of other specific fevers.

I shall confine my observations to the three diseases just named: septicæmia, relapsing fever, and splenic fever; merely remarking that, in regard to vaccinia, small-pox, sheep-pox, diphtheria, erysipelas, and glanders, the virus of these has been proved to consist of minute particles having the character of micrococci; and that, in regard to typhus, scarlet fever, measles, and the rest of the contagious fevers, their connection with pathogenic organisms is as yet a matter of pure inference. For further details, I must refer you to the able Reports of Dr. Braidwood and Mr. Vacher on the Life-history of Contagium, made on behalf of this Association, and published in the JOURNAL in the course of the past and present years.

SEPTICÆMIA.—We will first inquire how it stands with this doctrine in regard to traumatic septicæmia and pyæmia. You are all aware that foul ill-conditioned wounds are attended with severe, often fatal, symptoms, consisting essentially of fever of a remittent type, tending to run on to the formation of embolic inflammations and secondary abscesses.

The notion that septicæmia is produced by bacteria, and the *rationale* of the antiseptic treatment which is based thereupon, is founded on the following series of considerations.

1. It is known that decomposing animal substances—blood, muscle, and pus—develop, at an early stage of the process, a virulent poison, which, when injected into the body of an animal, produces symptoms similar to those of clinical septicæmia. This poison is evidently not itself an organism; it is soluble, or at least diffusible, in water, and it is capable, by appropriate means, of being separated from the decomposing liquid and its contained organisms. When thus isolated, it behaves like any other chemical poison; its effects are proportionate to the dose, and it has not the least power of self-multiplication in the body. To this substance, Dr. Burdon Sanderson has given the appropriate name of pyrogen. It is the only known substance which produces a simple uncomplicated paroxysm of fever—beginning with a rigor, followed by a rise of temperature, and ending (if the dose be not too large) in desquescence and recovery.

2. We know further, from the evidence I have laid before you, that decomposition cannot take place without bacteria, and that bacteria are never produced spontaneously, but originate invariably from germs derived from the surrounding media. We are warranted by analogy in regarding pyrogen as the product of a special fermentation taking place in decomposing albuminoid mixtures, but we cannot name the particular organism nor the particular albuminoid compound which are mutually engaged in the process.

3. In the third place, we know that when a wound becomes unhealthy, as surgeons term it, the discharges become offensive—in other words, decomposed—and when examined under the microscope they are found to swarm with organisms resembling those found in all de-

composing fluids. Meanwhile the patient becomes feverish, and suffers from the train of symptoms which we call septicæmia.

It is a natural inference that what takes place in decomposing blood or muscle in the laboratory takes place also in the serous discharges and dead tissues of the wound. These become infected from the surrounding air, or from the water used in the dressings, with septic organisms: on that follows decomposition and the production of the septic poison, or pyrogen; the poison is absorbed into the blood, and septicæmia ensues.

It was the distinguished merit of Lister to perceive that these considerations pointed to a means of preventing septicæmia. He argued that if you could prevent the access of septic organisms to the wound, or destroy them there, you would prevent decomposition, prevent the production of the septic poison, and thus obviate the danger of septicæmia. It is not within the scope of this address to describe the means by which Lister attained this object, still less to pass judgment on his practice, but I may be permitted to express my belief that the principle on which the treatment is founded is unassailable.

We should probably differ less about the antiseptic treatment if we took a broader view of its principle. We are apt to confound the principle of the treatment with Lister's method of carrying it out. The essence of the principle, it appears to me, is not exactly to protect the wound from the septic organisms, but to *defend the patient against the septic poison*. Defined in this way, I believe that every successful method of treating wounds will be found to conform to the antiseptic principle, and that herein lies the secret of the favourable results of modes of treatment which at first sight appear to be in contradiction to the antiseptic principle. Take, for example, the open method of treating wounds which is sometimes compared in its results with Lister's method. What is this treatment but another way (only less ideally perfect than Lister's) of defending the patient against the septic poison? Because, if the surgeon succeeds in providing such free exit for the discharges that there is no lodgment of them in the wound, either they pass out of it before there is time for the production of the septic poison, or if any be produced, it escapes so quickly that there is not enough absorbed to provoke an appreciable toxic effect.

Before we can understand the pathology of septicæmia we must have clear ideas on the relation of septic bacteria to our bodies. We see in our laboratories that dead animal tissues, when exposed to ordinary air or ordinary water, invariably breed septic organisms; in other words, contact of the septic germs with the dead tissues never fails to produce successful septic inoculation. But it is quite otherwise with the same tissues when alive and forming part of our bodies. You cannot successfully inoculate the healthy tissues with septic bacteria. It has been proved over and over again that these organisms, when separated from the decomposing medium in which they grow, can be injected in quantity into the blood or tissues of a healthy animal, or applied to a sore on its skin, without producing the least effect. The healthy living tissues are an unsuitable soil for them; they cannot grow in it; or, to put it in another way, ordinary septic bacteria are not parasitic on the living tissues.

This fact is of fundamental importance in the discussion of the pathology of septicæmia. We have a familiar illustration of its truth in the now common practice of subcutaneous injection. Every time you make a subcutaneous injection you inject septic germs into the tissues. I had the curiosity to test this point with the morphia solution used for this purpose in the Manchester Infirmary. I injected five drops of this solution into four flasks of sterilised beef-tea which had remained unchanged in my room for several months, taking care to avoid any other source of contamination. In forty-eight hours they were all in full putrefaction. But we know that no such effect follows when similar injections are made into the bodies of our patients.

It seems also probable that septic organisms enter constantly into our bodies with the air we breathe and the food we take; they pass, presumably, like any other minute particles, through the open mouths of the lymphatics and lacteals, and penetrate some distance into these channels; they certainly come in contact with the accidental cuts, sores, and scratches which so often bedeck our skins. Notwithstanding all this, our bodies do not decompose; indeed, if ordinary septic organisms could breed in the living tissues as they do in the same tissues when dead, animal life would be impossible, every living creature would infallibly perish. How these organisms are disposed of when they do enter our bodies accidentally, as it were, in the various ways I have suggested, we cannot say; we can only suppose that they must speedily perish, for we find no traces of them in the healthy blood and healthy tissues.*

Bearing in mind, then, that ordinary septic organisms cannot breed in the living tissues, unless, at least, they are reduced to near the moribund state; bearing also in mind that there is a sharp distinction to be drawn between the septic poison and the organisms which generate it, we are in a better position to consider the course of events in a wound, which leads on to septicæmia and pyæmia. What probably takes place is this: An unprotected wound receives infection from the septic organisms of the surrounding media. If the discharges are retained in the sinuosities of the wound, decomposition of them sets in with production of the septic poison. This is absorbed into the blood, a toxic effect follows, and septicæmia is established. As this effect increases with the continuous absorption of the poison, the vitality of the system is progressively lowered, and especially the vitality of the tissues bordering the wound, which may be topically affected by the poison which percolates through them. These tissues at length become moribund or die outright; the septic organisms then invade and breed in them, more septic poison is produced and absorbed; the toxæmia becomes intense, embolic centres of inflammation and suppuration are formed, and the end comes. In all this history there is no necessity to assume, nor even a probability, that septic organisms invade, or at least multiply in, the blood. They may do so at the near approach of death, but scarcely before that period.

In the course of traumatic septicæmia there sometimes occurs an event of great importance which imparts a new feature to the disease; I mean *infectiveness*. How this arises is a matter of speculation. To me it appears probable that, under a certain concurrence of conditions in and about the wound, a modification takes place in the vital endowments of the septic organism, whereby it acquires a parasitic habit, which enables it to breed in tissues of degraded vitality or even in the healthy tissues, and in this way to produce the infective endemic pyæmia which we sometimes witness in the wards of our large hospitals.* I shall develop this idea more fully by and bye.

Before leaving the subject of septicæmia, I may allude to the possibility of wounds being infected with septic organisms from within. As a rare occurrence, I am inclined to think that this is possible, and that it may account for the occasional alleged infection of protected wounds. From an observation by Chauveau, it may be inferred that septic organisms, when injected directly into the blood, are able to survive for two or three days, although unable to breed there.† It is conceivable that occasionally a septic germ entering the body in some of the ways which have been suggested may escape destruction and pass into the blood and lurk there awhile, and finding by chance some dead tissue or liquid within its reach, may multiply therein and produce septic effects. Such a contingency, if it ever occur, must be very rare, and would not appreciably detract from the value of the antiseptic mode of dressing wounds.

RELAPSING FEVER.—In 1872, Dr. Obermeier of Berlin discovered minute spiral organisms (spirilla) in the blood of patients suffering from relapsing fever. This discovery has been fully confirmed by subsequent observations. The organisms are found during the paroxysms; they disappear at the crisis; and are absent during the apyrexial periods.

The drawings represent the various appearances presented by these little parasites. They consist of spiral fibrils of the most extreme tenuity, varying in length from two to six times the breadth of a blood corpuscle. In the fresh state they move about actively in the blood. They have not been detected in any of the fluids or secretions of the body except the blood, nor in any other disease than relapsing fever. In form and botanical characters they are almost identical with the *Spirochaete plicatilis* of Ehrenberg (*Spirillum* of Dujardin) a species of bacteria found in dirty water and occasionally in the mucus of the mouth. Cohn designated the variety found in the blood *S. Obermeieri*, in honour of its discoverer.

In the beginning of the current year, Dr. Heydenreich‡ of St. Petersburg, published an elaborate monograph on this subject, which, I think, goes far to reconcile the conflicting statements and opinions put forth by previous writers in regard to the connection of the spirilla with relapsing fever. It is based on forty-six cases; these cases were studied with the most minute care; the blood was examined, and the

found that portions of the liver and kidneys removed from the body without extraneous contamination, produced bacteria, contrasting in this respect with the blood and muscles.—BRITISH MEDICAL JOURNAL, February 13th, 1875.

* Such a modification or "variation" might be correlated with a modification of the ferment action, whereby a more virulent septic poison is produced. Would not such a view explain the sudden intensification of the infecting virus which was found by Chauveau and Dr. Sanderson in their experiments on infective inflammations?

† Comtes Rendus, 1873, p. 1092.

‡ L. Heydenreich, *Ueber den Parasiten des Rückfallstypus*; Berlin, 1877. He gives a good résumé of the literature of the subject.

* Exception must apparently be made in regard to the tissues and organs in the immediate vicinity of the absorbent surfaces. Both Klebs and Burdon Sanderson

temperature observed from two to six times each day. Altogether, over a thousand examinations of the blood were made.

Relapsing fever still prevails extensively in certain districts of Germany and Russia, but it is almost a forgotten disease in this country; and probably the majority of those in this room have never seen a case. It will, therefore, not be amiss if I remind my hearers, and myself, of its principal features. It is a contagious epidemic fever characterised by a sharp paroxysm of pyrexia, which lasts about a week, and ends with a severe critical sweating. This is succeeded by an intermission, also of about a week, during which the patient is apyrexial; then follows a second paroxysm, or relapse, which lasts four or five days, and ends, as before, in a critical sweating. Recovery usually follows the second paroxysm, but not unfrequently a third paroxysm occurs, and sometimes a fourth.

The paroxysms are occasionally broken by remissions or pseudo-crises; and the apyrexial periods are sometimes interrupted by slight temporary rises of temperature.

Bearing these characteristics in mind, we shall be able to understand the significance of Heydenreich's observations. He found that every rise of temperature, whether that of the true paroxysm, or that following a pseudo-crisis, or those occurring during the intermissions, was invariably preceded by the appearance of spirilla in the blood. They disappeared entirely shortly before the crisis, and remained absent during defervescence and the subsequent apyrexial periods. During the whole of the main paroxysms spirilla were usually to be found in the blood, but their number varied in the most puzzling manner from day to day. One day they were abundant, the next day they were scanty, and the day after again abundant; they even varied at different hours of the same day; sometimes they vanished altogether for a time, and then reappeared in vast numbers a few hours later. Throughout these variations the temperature remained steadily high, or with only slight or moderate oscillations.

These discrepancies had been observed by previous inquirers, and had led some to doubt whether the spirilla had anything to do with the virus of relapsing fever; but a happy idea suggested itself to Heydenreich which seems capable of explaining them.

He found that when a little blood containing spirilla was abstracted from the patient and kept at the ordinary temperature of the room, the organisms lived in it for several days; but if the blood was placed in an incubator and maintained at the normal temperature of the body, they died in from twelve to twenty hours, and if the temperature was kept up to fever heat (104 deg. F.) their life was still shorter; they only survived from four to twelve hours. This led him to the conjecture that during the main paroxysm, not one, but several successive generations of spirilla were born and died before their final disappearance at the crisis. He surmised that in the usual course, the broods would overlap each other more or less, the new brood making its appearance before the last survivors of the old brood had passed away. This explained the variable number of spirilla found on different days and different hours of the same day. Sometimes the old brood would have altogether perished before the new brood reached maturity; this explained the occasional temporary absence of spirilla from the blood; it also explained the remissions or pseudo-crises sometimes observed in the course of the paroxysms. So precise was the correspondence found to be between the appearance of the spirilla and a subsequent rise of temperature, that Heydenreich was able to predict with certainty, during the apyrexial periods, the approaching advent of a transient rise of temperature from the re-appearance of spirilla in the blood, although at the time the patient presented no other indication of what was about to happen.

If these observations are to be relied on—and they appear to have been made with the most scrupulous care—we are led to the conclusion that the spirilla are the actual virus of relapsing fever.

The same conclusion is also strongly indicated by the results of inoculation experiments. Relapsing fever is easily communicated to a healthy person by inoculation with the blood of a patient suffering from the disease. Experiments made in Russia on individuals who voluntarily submitted themselves to this practice, show that the blood is only infective during the paroxysms, but not at the crises nor during the apyrexial periods. None of the fluids or secretions of the body except the blood are infective. All this shows that the virus is intimately associated with the spirilla, and is absent or present in exactly the same circumstances as the latter.*

The occasionally observed vanishing and re-appearance of the spirilla

during the paroxysm, without a possibility of new infection, seems to indicate that when the spirilla disappear they leave behind them something in the nature of seed or spores, from which the new brood springs forth. Ocular evidence of such germs is, however, still wanting. Several observers have noticed minute particles in the blood of relapsing fever which might pass for spores, and Heydenreich observed that some of the spirilla had a dotted appearance. But hitherto all efforts to cultivate the spores out of the body have failed, and their power of developing spores is more an inference than a demonstration.

SPLENIC FEVER.—The first trustworthy observation of the presence of organic forms in an infective disease was made in splenic fever. This formidable disorder attacks sheep, cows, and horses, and is not unfrequently fatal to man. In 1855, Pollender discovered minute staff-shaped bacteria in the blood of splenic fever. This discovery was confirmed in a very extensive series of researches by Brauell, and has been corroborated by Davaine and other inquirers in France.

The bacterium of splenic fever is a short, straight, motionless rod, about as long as the breadth of a blood-corpuscle, and, so far as is known, it exists in no other form in the living body. It is found, besides the blood, in the spleen, in the lymphatic glands, and in some other tissues. That this organism is the true virus of splenic fever has long been probable; and the labours of Davaine, Bollinger, Tiegel, Klebs, and, most of all, of Koch, have removed the last doubts on the subject. The work done by Koch is not only valuable as a triumphant demonstration of a disputed pathological question, but is noteworthy as a model of patient, ingenious, and exact pathological research.

We here come across an example of scientific prescience on the part of two distinguished men which is worth notice. It had been remarked by several observers that the contagium of splenic fever, as it existed in the blood, was comparatively short-lived and fugitive, but that, under some unexplained circumstances, the contagium was very persistent, and lurked for years in stables and other places where cattle were kept. Dr. Burdon Sanderson, writing in 1874, inferred from this circumstance that the organisms of splenic fever must have two states of existence; namely, that of the perishable bacteria found in the blood and some other more permanent form, like seeds or spores, in which they were capable of surviving for an indefinite period. In like manner, Professor Cohn, guided by the botanical characters of the rods found in the blood, classed them in that group of bacteria named by him *Bacillus*; and, as he had observed that all the *Bacilli* produced spores, he inferred that the *Bacillus anthracis*—for so he named the bacterium of splenic fever—would also be found to produce spores. These previsions were proved by the researches of Koch to be perfectly exact.

The following is a brief abstract of those points in these researches which chiefly concern us.

Koch found that mice were peculiarly susceptible to the virus of splenic fever. The minutest particle of the fresh blood or spleen of an infected animal infallibly produced the disease when brought into contact with the living tissue of the mouse. He found further that he could cultivate the organisms artificially outside the body. He proceeded in the following manner. He placed a speck of the spleen containing the rods on a glass slide in a drop of the blood-serum of the ox, or a drop of the aqueous humour of the eye of the same animal, and covered it with a piece of thin glass. He then placed the slide in an incubator maintained constantly at the temperature of the body, and examined the preparation from time to time under the microscope. In a couple of hours, he observed that the rods began to lengthen, and in a few hours to grow into long threads. These threads, after growing to twenty or a hundred times the length of the original rods, began by and by to assume a dotted appearance. The dots gradually increased in size and distinctness until, after the lapse of fifteen or twenty hours from the beginning of the experiment, they acquired the appearance of strongly refractive oval bodies, which were placed at regular intervals along the threads. Finally, the threads broke down, and the oval bodies, which could be nothing else than spores, were set free and sank to the more depending parts of the drop. If the supply of nutriment were then exhausted, the process ended here, and the spores remained permanently unchanged; but, if additional nourishment were provided, the new spores were seen presently to elongate into rods, exactly resembling those originally existing in the blood or spleen. If the conditions were favourable, the new rods, after a period of rapid multiplication, in their turn entered on the formation of a new generation of threads and a new generation of spores. The figures represent the successive phases of this short and simple, but perfectly definite, life-history as they were actually seen to occur under the lens of the microscope.

* See a paper by Motschutowsky, in the *Centralblatt für die Medicinischen Wissenschaften*, 1876, p. 193. During the paroxysm the blood was infective, whether spirilla were detected in it or not. This agrees with Heydenreich's theory, that their occasional apparent absence during the paroxysm is due to their being incompletely developed, or immature, and therefore unrecognisable under the microscope.

The next point was to test the pathogenic activity of the rods and spores cultivated in this artificial manner. This was done by introducing minute quantities of the rods, or of the spores alone, into a small incision made in the skin of a mouse. Speedy death from splenic fever occurred in every instance. Koch found, without exception, that, if the tested material produced threads and spores in the incubator, it also produced splenic fever when inoculated into the mouse; and, on the contrary, if no such growth and development took place in the incubator, the tested material produced no effect when inoculated into the mouse. Proof could go no further: the infection absolutely followed the specific organism; it came with it, it went with it. These observations were repeated with the strictest precautions at the Physiological Institute at Breslau, under the eyes of Professor Cohn and other competent observers, who fully corroborated their exactness.

The variable duration of the activity of the contagium of splenic fever was now explained. Koch found that the rods had only a comparatively fugitive vitality; they lost their infective power generally in a few days; at the most, in about five weeks. But the spores retained their infective activity for an indefinite period, in spite of all kinds of maltreatment. They could be reduced to dust, wetted and dried repeatedly, kept in putrefying liquids for weeks, and yet, at the end of four years, they still displayed an undiminished virulence.

Cohn calls attention to the fact that the organism of splenic fever is identical in form and development with the *B. subtilis*. The only difference he could detect between them was, that the rods of *B. anthracis* are motionless, while those of *B. Subtilis* exhibit movements. The figures you see before you might be indifferently labelled *B. subtilis* or *B. anthracis*, and yet one of these organisms is a harmless saprophyte and the other a deadly contagium. We have likewise seen that the spirilla of splenic fever are morphologically similar with the *Spirochaete plicatilis*. We have further seen that there is ground for the assumption that the infective agent in contagious septicæmia is the common bacterium of putrefaction, but modified in such a way as to have become endowed with a heightened capacity for growing in the healthy tissues. Do not these remarkable coincidences point to a natural explanation of the origin of contagia? If contagia are organisms, they must necessarily possess the fundamental tendencies and attributes of all organised beings. Among the most important of these attributes is the capacity for "variation" or "sporting". This capacity is an essential link in the theory of evolution; and Darwin brings forward strong grounds for the belief that variation in plants and animals is not the result of chance or caprice, but is the definite effect of definite (though often quite obscure) causes. I see no more difficulty in believing that the *B. anthracis* is a sport from the *B. subtilis* than in believing, as all botanists tell us, that the bitter almond is a sport from the sweet almond—the one a bland innocuous fruit, and the other containing the elements of a deadly poison.

The laws of variation seem to apply in a curiously exact manner to many of the phenomena of contagious diseases. One of these laws is the tendency of a variation, once produced, to become permanent and to be transmitted ever after with perfect exactness from parent to offspring; another and controlling law is the tendency of a variation, after persisting a certain time, to revert once more (under altered conditions) to the original type. The sporting of the nectarine from the peach is known to many horticulturists. A peach-tree, after producing thousands and thousands of peach-buds, will, as a rare event and at rare intervals, produce a bud and branch which ever after bear only nectarines; and, conversely, a nectarine at long intervals, and as a rare event, will produce a branch which bears only peaches ever after. Does not this remind us of the occasional apparent sporting of diphtheria from scarlet fever? My friend Dr. Ransome, who has paid so much attention to the laws governing the spread of epidemics, relates the following instance:—A general outbreak of scarlet fever occurred at a large public school. One of the masters who took the infection exhibited diphtheritic patches on the throat. This patient was sent to his own home in Bowdon. Six days after his arrival, his mother was attacked, not with scarlet fever, but with diphtheria; though there were no cases of diphtheria at the time, neither at the school nor in Bowdon.*

Take another illustration: cholera suddenly breaks out in some remote district in India, and spreads from that centre over half the globe. In three or four seasons, the epidemic dies away and ceases altogether from among men. A few years later, it reappears and spreads again, and disappears as before. Does not this look as if the cholera virus

were an occasional sport from some Indian saprophyte, which by variation has acquired a parasitic habit, and, having run through countless generations, either dies out or reverts again to its original type? Similarly, typhoid fever might be explained as due to a variation from some common saprophyte of our stagnant pools or sewers, which, under certain conditions of its own surroundings, or certain conditions within the human body, acquires a parasitic habit. Having acquired this habit, it becomes a contagious virus, which is transmitted with its new habit through a certain number of generations; but finally, these conditions ceasing, it reverts again to its original non-parasitic type.

In regard to some contagia, such as small-pox and scarlet fever, it might be said that the variation was a very rare one, but also a very permanent one, with little or no tendency to reversion; while others, like erysipelas and typhoid fever, were frequent sports, with a more decided tendency to reversion to the original type. In regard to some pathogenic organisms, it might be assumed that the parent type had disappeared, and the parasitic variety only remained—just as the wild parents of many of our cultivated flowers and vegetables have disappeared, leaving behind them only their altered descendants.

How aptly, too, this view explains what used to be called the "Epidemic Constitution", and the hybrid forms and subvarieties of eruptive and other fevers.

I must not pursue this vein further. I have said enough to indicate that this conception enables us—if it does nothing else—to have coherent ideas about the origin and the spread of zymotic diseases.

In applying the doctrine of pathogenic organisms—or pathophytes, as they might be termed—to the explanation of the phenomena of infective diseases, we must be on our guard against hard-and-fast lines of interpretation. So far as our very limited knowledge now extends, the pathophytes hitherto discovered all belong to that group of the fungi which are called bacteria. Now, fungi have two marked characteristics, namely, the tendency to assume the parasitic habit, and the possession by some of them of a special ferment action. Both these characteristics may bear a part in the action of pathogenic organisms. In the complex phenomena of septicæmia such would appear to be the case—a poisonous ferment-product first intoxicates the system, and then the organisms themselves prey upon the dead or moribund tissues.

There is, as Dr. B. Sanderson has pointed out, a marked distinction to be drawn between those common processes of infective inflammation which are shared in by animals generally—such as septo-pyæmia, erysipelas, and the diphtheritic process—and those specific contagia which are strictly confined, like ordinary parasites, to particular species. There is nothing in all nature more wonderful than the intimate and subtle nexus which unites a parasite to its host. A hundred examples might be given. Even different varieties or races of the same species have different and exclusive parasites. It would seem as if this nexus depended on some delicate shade—a *nuance*—something like an odour, or a savour, or a colour, rather than on differences of structure or chemical composition. The same minute correlation is seen in specific contagia—all are strictly confined to one or a few species. Vaccinia is confined to man, the horse, and the cow; scarlet fever is confined to man, and perhaps the swine; most of our specific diseases are absolutely confined to man. The human and ovine small-pox, although so wonderfully similar, are not intercommunicable. I am, therefore, inclined to believe that, in regard to specific contagia, we shall find more guiding analogies in parasitism than in fermentation. Our information at present is, however, so defective that it is not wise to enter into further speculations on this subject.

Gentlemen, I have brought my task to a conclusion. I believe that the doctrine of a contagium vivum is established on a solid foundation; and that the principle it involves, if firmly grasped in capable hands, will prove a powerful instrument of future discoveries. And let no man doubt that such discoveries will lead to incalculable benefits to the human race: our business in life is to do battle with disease, and we may rest assured that the more we know of our enemy the more successfully we shall be able to combat him.

SCARBOROUGH.—The births in 1876 were 768 and the deaths 550; but of these 17 deaths occurred amongst visitors from various diseases, and 12 of non-residents in the workhouse, making 521, which give a death-rate of 19.51 per 1,000, or, with the visitors, 20.14, which is higher than before. There were 69 deaths from zymotic diseases, but not one of small-pox; and the Vaccination Act appears to be well carried out. There was a large mortality from diarrhoea, which Dr. Taylor attributes chiefly to improper feeding and nursing. There are two important meteorological tables attached, showing the average monthly range of temperature to have been 26.7 deg., the mean daily range 8.7 deg., and the mean daily temperature 48.3 deg. Fahr. The rainfall was 32.15 inches.

* Complex cases of mingled scarlet fever and diphtheria are sometimes seen. Similarly the peach-tree will occasionally, among a multitude of ordinary fruit, produce one fruit of which one-half has the peach character and the other half the nectarine character.—Darwin.