INTRODUCTORY ADDRESS

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BY

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A RECORD OF EXPERIMENTS ON FERMENTATION.

GENTLEMEN,—In making my first appearance as teacher in King's College, I cannot refrain from expressing my deep sense of the honour conferred upon me by the invitation to occupy the chair which I now hold; and, at the same time, my earnest hope that the confidence thus reposed in me may not prove to have been misplaced.

In considering how I could best discharge my duty as the person selected to deliver the Introductory Address of the Medical Session, I have felt that two courses were open to me: either to spend the short but important time at my disposal in an endeavour to convey to the student some sense of the exalted privileges, and correspondingly high responsibilities, of the beneficent calling to which he proposes to devote himself, or to treat on some special subject, in the hope that I might say something which should have interest and, if possible, even instruction, not only for the student, but also for the eminent men whom I have the honour to see around me. The latter is the course which I have decided to follow, and the subject which I have selected is a short account of an inquiry in which I have been engaged in the interval between the cessation of my official duties in Edinburgh and their commencement here. The object of that investigation was to obtain, if possible, some positive and definite knowledge of the essential nature of a class of phenomena which interest alike the physician, the surgeon, and the accoucheur. I allude to the changes in organic substances which are designated by the general term fermentation.

In medicine, the large class of diseases termed zymotic derive their name from the hypothesis that their essential nature is fermentative. In obstetrics, puerperal fever, the most frequent cause of disaster after childbirth, is now regarded by many of the highest authorities as likewise due to fermentative disorder; and, in surgery, among the various causes which may disturb a wound, we know that by far the most frequent in operation, and the most pernicious agent in its effects both upon the wounded part and upon the constitution, is putrefactive fermentation. If this be so, it is clear that to understand the nature of fermentation must be a matter of the very highest importance, with a view to curing or preventing the various evils to which I have alluded.

What, then, do we mean by fermentation? I shall best approach the answer to this question by giving an example. Rather more than a week ago, I witnessed in the north of Italy the time-honoured practice of treading grapes in the wine-vat. I was told that the juice would within twenty-four hours boil, as it was said, over the vats into which it was introduced; in other words, that the sugar of the grape-juice would within that short time be so converted into alcohol and carbonic acid gas, that the carbonic acid gas, by its ebullition, would cause sufficient frothing to produce the effect to which I have referred. This conversion of the sugar of the grape into alcohol and carbonic acid gas is accompanied by the development of a microscopic organism, the yeast-plant, or, to continue the old nomenclature, *Torula cerevisia*, consisting of microscopic cells multiplying by pullulation, as indicated in this rough diagram. Now, it is, I believe, universally admitted that the alcoholic fermentation of grape-sugar is due to the growth of the yeast-plant. M. Pasteur thinks that he has traced the origin of the yeast-plant in the juice of the grape to a minute fungus adhering to the outside of the skin of the grape. Be this as it may, it is admitted on all hands that the alcoholic fermentation is caused by the growth of the yeast-plant. So long as the juice of the grape is protected by the skin of the berry, no fermentation occurs; but, as soon as it escapes from that protection, the organism, by its development, induces the fermentation. Nor is it by any means exclusively in the natural juices of fruits that such fermentation is induced. Any sugary solution, provided it contains, besides the sugar, other ingredients requisite for the nutrition of the yeast-plant, will serve as

palabulum for the yeast-plant, and in this case the yeast-plant will give rise to the fermentation. Here is a glass containing what is termed Pasteur's solution, a solution devised by M. Pasteur for the very purpose of affording nourishment to the yeast-plant and other minute organisms. This was prepared on September 10th in a flask purified by heat, covered over with a pure cotton cap, which permits the entrance of air, but does not permit the entrance either of the yeast-plant or of any other form of dust. The Pasteur's solution, of itself containing, besides sugar, ammoniacal and earthy salts for the nutrition of the fungus, was heated to about the temperature of boiling water, so as to destroy any organisms that might exist in the water. The result is, that it continues perfectly unchanged, just as it was on September 10th; but, if we were to add to it a little of the yeast-plant from fermenting grape-juice, we should find that, at the temperature of summer weather, this would very soon be in a state of free fermentation at the same time that the yeast-plant would multiply. This, then, is a typical instance of fermentation. We have an active agent termed the ferment, which ferment is capable of self-multiplication. That I believe to be the essential property of a true fermentation. There is an active principle termed the ferment, which ferment has the faculty of self-multiplication. Now, in this particular case, I have already said it is admitted on all hands that the yeast-plant is the cause of fermentation. Persons may differ as to how the development of the yeast-plant gives rise to the resolution of the sugar into the alcohol and carbonic acid gas; but all now agree that, somehow or other, the yeast-plant causes the fermentation. Now, is this so in all cases, in the case of all fermentations? Are all true fermentations caused by the development of organisms? That, gentlemen, is the question which it is desirable that we should be able to answer.

Take, for example, the case of the putrefactive fermentation of blood. We all know that, if blood be shed from the body into any vessel without special precautions, in a few days it putrefies. The bland nutrient liquid, soon after leaving its natural receptacle, becomes foul, acid, and poisonous: a change fully as striking as the change which sugar undergoes in the alcoholic fermentation. Here we have a glass into which blood was received with special precautions. In the first place, the glass, covered, as you see, with a glass cap and a glass shade, with a view of preventing the access of dust, and standing upon a piece of plate-glass, had been heated to about the temperature of 300 deg. Fahr., and cooled with an arrangement that insured the filtering of the air from its dust—the air that entered during cooling—so that we were perfectly sure that the glass contained no living organisms.

Then, in the second place, the glass had been charged from a flask like this. It contains, as you see, a glass tube introduced into it; it is stuffed well with cotton-wool between the neck of the flask and the tube, there is a piece of cotton-wool over the end of the tube, and another piece is tied securely over the spout of the flask. The flask so arranged was heated just as the glass had been heated. It is not necessary to heat so high as to singe the cotton. Heat far short of this is adequate, according to my experience, to make perfectly sure that you destroy all living organisms. The flask having been thus prepared, the jugular vein of an ox was exposed, with precautions against the entrance of anything putrefactive, and, the cotton cap having been taken off from the end of the tube, the jugular vein was slipped over the tube, tied on, and then the hand of the assistant, who previously restrained the flow of blood, being relaxed, blood was permitted to flow into the flask. Then, before coagulation had time to take place, this and various other glasses were charged after the removal of the cotton cup from the end of the spout. Now, the first thing that may strike you is the remarkable fact that this blood-clot has not undergone any contraction. One of the earliest things that your professor of physiology will have to teach the junior students will be that blood, after coagulation, contracts; that the blood-clot contracts; that the fibrin is pressed out. But here no such thing has taken place. There has been no shrinking of this clot, no pressing out of the fibrin, and I venture to say that there is no one here, at least I think it is unlikely that there is anyone here except myself, who has seen such a phenomenon, illustrating how, when the most familiar objects are placed under new circumstances, the most unexpected results will arise. Now, this is a matter of very considerable interest with reference to the behaviour of blood-clots inside the body in wounds and so forth. However, that is not the point to which I wish now to draw your attention. The point to which I wish to draw your special attention is, that this blood, although it has been six weeks in this glass, without any close fitting of the glass shade or the glass cap, has not putrefied. The air is perfectly sweet, perfectly free from odour.

Now, gentlemen, this, without going further, is a very important matter. It proves that the blood has no inherent tendency to putrefaction. It further proves that the oxygen of the air is not able to

cause the blood to putrefy, as used to be supposed. There was a time—the effect is still seen to a certain extent—when the dark venous colour of this blood-clot gave place to the crimson colour of arterial blood in a gradually deepening band from above downwards. We still see some of the red colour remaining, though now the converse effect has begun to take place. That florid redness, then, gentlemen, showed that the oxygen of the air was in reality acting upon the blood, yet it did not putrefy. Now, if I were to take a little morsel of already putrefied blood, say, upon the end of a needle, and touch with it this clot of blood, putrefaction would, in the course of a very short time, spread throughout the mass. Exactly as in the case of alcoholic fermentation under the influence of a yeast-plant would the fermentation spread.

Putrefaction, then, is a fermentation, a true fermentation, characterised by the power of self-propagation of the ferment. Then, gentlemen, if we examine microscopically, we find in the putrefying blood, as we found in the fermented grape-juice, microscopic organisms, termed bacteria from their rod-shape, which we have here represented on the same scale as we had the yeast-plant; some of different sizes, very much more minute than the yeast-plant, and commonly endowed with a remarkable power of locomotion. I say that, in the putrefying blood, we find these organisms developing *pari passu* with the fermentation.

Now, the question is, Are these bacteria the cause of the putrefactive fermentation, or are they merely accidental concomitants? These are two views which are entertained at the present day by men of high eminence. It may be said, "Why should there be any doubt that the bacteria are the cause of the putrefactive fermentation, any more than there is a doubt that the *Torula cerevisiæ* is the cause of the alcoholic?" Well, one reason I believe to be that the bacteria are so exceedingly small. They are not so easily defined. We cannot get them in a mass as we can get a mass of yeast; at least without a great deal of trouble; and, besides that, they occur very similar in appearance in a great number of different fermentations. There is, therefore, so far some colour for doubting whether bacteria are the cause of a special fermentation, like this putrefaction. Then there is another ground justifying such a view; for certain it is that organic substances are liable to extremely remarkable alterations, decompositions, under the influence of agents which are endowed with no life at all. As good an example of this as we can take is what occurs in the bitter almond when it is bruised with water. You all know what takes place under those circumstances; that there is prussic acid developed, and essential oil of almonds, and other materials. Now, these did not exist beforehand in the bitter almond, but they are the result of the mutual action upon each other of two constituents of the bitter almond, neither of which was hydrocyanic acid, nor oil of bitter almonds, etc. These two constituents are termed emulsin and amygdalin. Amygdalin is a crystallisable substance, and can be obtained separately. Emulsin, though not obtained in a state of crystallisation, can be obtained separately. Till these two materials are in a state of solution in water, they do not act upon each other, upon the bitter almond at all; but, as soon as they are in watery solution, the emulsin so acts upon the amygdalin that the amygdalin becomes broken up into the constituents to which I have referred. This is an exceedingly remarkable fact. Undoubtedly, the emulsin is dead; there is nothing living about it. It is not an organism. It is obtained by a process of alcoholic extraction and so forth. It is thoroughly a chemical substance, a merely dead substance, if we may so speak, and yet it does produce this remarkable effect upon the amygdalin. But, when we come to consider this case, we find that this process, remarkable as it is, lacks the true character of genuine fermentation, that of the faculty of self-propagation of the ferment. Liebig himself, who was the great advocate of the doctrine of so-called chemical ferment, and who discovered this action of emulsin on amygdalin, pointed out, and showed by irrefragable evidence, that the emulsin does not undergo any multiplication; not only so, but that, after a while, it so happens that the emulsin loses the property of acting on the amygdalin; but, for a considerable time, it continues to act upon it without undergoing apparently either increase or diminution of its bulk. It may be called a resolvent, the amygdalin being the resolved material.

There are other cases equally striking that might be mentioned, not only in the chemistry of vegetables, but in the chemistry of our own bodies. There exists, for instance, in the saliva a material called ptyalin, which has a remarkable power of acting upon starch. In the gastric juice, there is a material called pepsin, which has a remarkable power undoubtedly of acting on albuminous materials, fitting them for solution in digestion. But here again we find, when we come to consider the matter, that there is no evidence whatever that either pepsin or ptyalin is capable of self-multiplication. Each is secreted for the

purpose and in the quantity in which it is required, but it has no faculty of self-multiplication; and I believe, if you search through the whole range of organic chemistry, you will not find a single recorded instance where any ferment, so-called, destitute of life has been proved to have the power of self-multiplication. At the same time, gentlemen, though this is the fact, I believe I am correct in stating that it may be admitted that the thing might be theoretically possible. It is conceivable, for instance, that a resolvent, if we may so speak, of comparatively simple constitution might, by its action upon a resolvable compound, resolve it into substances, one of which should itself be the resolvent, and, if that were so, the process might go on *ad infinitum*. That is conceivable; and even, gentlemen, if it were not conceivable, although we have no instance of the kind on record, yet we have persons in high authority, as teachers both of physiology and of pathology, maintaining this view: that probably, under the circumstance, for instance, of putrefactive fermentation, the bacteria are mere accidental concomitants; but the real essential agent in the putrefaction is not an organism at all, but some so-called chemical ferment destitute of life. I say, so long as we have authorities maintaining such a view, it is our duty, if we can, to disprove it; and it has been with this object that the investigations of the last two months, to which I have referred, have been conducted.

I may say that, as regards the putrefactive fermentation, we have already evidence in the flask and in the glass that I have shown you (the flask also has no putrefactive odour emanating from it), that blood has in itself no inherent tendency to putrefy. It must receive something from without, and that something is not mere oxygen. Mere oxygen will not do; mere water will not do. Blood and water constitute a mixture highly putrescible, very much more liable to putrefaction than blood itself. But here we have had mixed with water the contents of a glass like this, only that the water had been previously boiled, so as to kill any organisms in it; boiled under the protection of a cotton cap, and then, the cotton cap being raised, careful provisions (into which I must not enter) against the entrance of dust being taken, the clot was spooned into the water; a fresh cotton cap, perfectly pure, was put on, and so we got, I believe for the first time, a permanent cold watery extract of blood, and here it retains the same brilliant clearness that it had in the first instance, more than a month ago.

The special process of fermentation which I have been investigating has not been the putrefactive, but one which seemed to me more convenient for the purpose, the lactic fermentation, the fermentation by means of which milk sours and curdles, by means of which the sugar of milk, instead of being converted as grape-sugar into alcohol and carbonic acid, is converted into lactic acid; a curious instance of a chemical alteration. The chemical composition, as regards the proportions of the three elements, carbon, hydrogen, and oxygen, remains identically the same; but those of you who are chemists understand what I mean when I say the atomic weight of the lactic acid is one-fourth of the atomic weight of the sugar of milk. Each atom has been resolved into four simple atoms of lactic acid. Now, it may be naturally supposed, if you observe what happens in a portion of milk obtained from a dairy, that this is an absolute inherent tendency of the milk, this souring and curdling. If you get milk from a dairy and keep it long enough, it is certain to turn sour and curdle; then after a while, there comes a certain mould upon the surface, the *oidium lactis*, which constitutes the sort of bloom there is upon a cream cheese; then afterwards comes on, often simultaneously with the growth of this mould, the butyric fermentation, in which butyric acid is produced; and afterwards, if you keep the milk long enough, it will probably putrefy. When you see, time after time, specimens of milk, taken from various dairies, undergo this succession of alterations, you may be tempted to suppose that these were changes to which the milk was disposed from its own inherent properties as it comes from the cow's udder. The late eminent Professor of Chemistry in this College, Professor Miller, in his excellent work on Chemistry, states that the ferment of the lactic acid fermentation is the caseine of the milk. I am bound to say, however, in justice to Professor Miller, that he also adds that M. Pasteur has expressed his belief that there exists an organic living ferment which produces this fermentation; but Professor Miller does not profess to decide between these two opinions. On the contrary, his first statement, that the caseine is the ferment, might lead you to suppose that he inclines to the former view. If this were the case, as there is caseine always in the milk, there should always be the lactic acid fermentation. But it was pointed out long ago by M. Pasteur that, if you examine any specimens of souring milk with the microscope, you find little organisms. These, when you come to look at them carefully, you see to be obviously of the nature of bacteria. Bac-

teria may either have the faculty of motion or they may not. This particular bacterium is a motionless bacterium, so far as I know; still it has the essential nature of a bacterium: a microscopic fungus, multiplied by fissiparous generation, always by lines transverse to the longitudinal axis of the organism. I have ventured to give to this little organism the term *bacterium lactis*; for, gentlemen, no doubt there are different kinds of bacteria. The mere fact that they are minute must not make us shut our eyes to this fact. You sometimes hear bacteria spoken of as if they were all alike. The fact that some do not move and others do, is one indication of a difference. Another indication of a difference is, that some bacteria will thrive in a substance in which others cannot live. For instance, the *bacterium lactis* refuses to live at all, according to the more careful experiments I have been lately making, in Pasteur's solution; the very fluid provided by Pasteur for bacteria to live in, and for these *torulæ* and for fungi generally, that is a medium in which the *bacterium lactis* refuses to grow at all, although the majority of bacteria grow in it with rapidity. That is clear evidence that this is a different kind of bacterium from those which both move and thrive in Pasteur's solution. You will observe, also, it is somewhat peculiar in the form of the segments; they are oval, and not so rod-shaped as bacteria generally. These you will always find in milk when it is in the early stages of souring. This is a flask of boiled milk, prepared on August 27th. It has not coagulated; it has undergone none of the changes to which I have alluded. There has been no butyric fermentation, no *oidium lactis* has formed upon it, no putrefaction. This milk is as sweet as when it was first prepared. From this same flask, with precautions with which I will not detain you, I have charged various glasses. This has been charged for weeks: the milk remains fluid, you observe, although there is abundantly free access of air. The oxygen of the air and the caseine which still exist in the boiled milk have together been unable to bring about this lactic fermentation. As regards boiled milk, we have already sufficient evidence that the lactic fermentation is not something to which the boiled milk is spontaneously prone; it requires something to be introduced into it from without. Not only so, but, suppose you take a series of glasses of boiled milk like these, and introduce into them a series of drops of water, you will get fermentation in them. If you take, for instance, a drop as large as a quarter of a minim, you will have a fermentation in every one, and an organism in every one; but you will neither have, according to my experience, the lactic acid fermentation nor the *bacterium lactis*. You will have bacteria of other sorts, fermentation of other kinds.

Again, suppose you take a series of such classes, take off the glass shades and the glass caps, in different apartments and at different times, and expose the milk to the air-dust for half an hour; you will get fungi and bacteria of different sorts, but you will not get the lactic fermentation. According to my experience, you will not get the *bacterium lactis*; and thus it turns out, so far as boiled milk is concerned at all events, that the ferment that brings about this particular fermentation is a rare ferment. So far from boiled milk being spontaneously prone to the change, it requires something to be introduced from without, which is a rarity both in ordinary water and in ordinary air, and yet, undoubtedly, this is a true fermentation. If you were to take such a glass as this, and dip the point of a needle into a glass of souring milk, and touch with the needle point the edge of the milk, within two or three days it would be a sour clot. Then you should find, as certainly as I did, the *bacterium lactis* throughout the mass.

But then, it may be urged, indeed such arguments have been used, this may be very well for boiled milk, but how about unboiled? May it not be that, by boiling the milk, you have destroyed certain chemical substances, purely hypothetical we must admit, but which we do think likely to exist? It is very difficult sometimes to avoid an offensive expression. I do not at all wish to make use of one; but it may be, according to the views of some persons, that in the unboiled milk there may exist certain chemical substances prone to evolve into organisms by spontaneous generation, and prone to produce these and other fermentations; but which, by the act of boiling, we deprive of this tendency; and, therefore, with a view to meet this objection, the first part of my investigation was devoted to endeavouring to see whether or not milk, as it comes from the cow, really does or does not contain materials tending to the development of organisms or to fermentation of any kind.

An exceedingly simple experiment will probably serve to convince you to a considerable extent with regard to this matter. If you go to a dairy where there is also a cow-house, take a couple of clean bottles, and fill one with milk from the dairy and the other with milk direct from the cow in the cow-house, the milk obtained from the dairy will be certain to sour, but the milk that you get direct from the cow will very probably never sour at all. It will acquire a nasty bitter taste,

and will not have the *bacterium lactis* or the *oidium lactis*, but some other kinds of fungi. Well, now, a very simple experiment is enough to show that the lactic acid fermentation is not a change to which milk is spontaneously prone. If this be so, it occurred to me that, if we were to take more care in the experiment, and also to perform the experiment so as to take the milk into vessels previously purified, in small quantities, we might be able to get the milk not only without the lactic acid fermentation or the *bacterium lactis*, but without any fermentation or any bacterium, or any sort of organism. Accordingly, I arranged a number of little glasses like these, and little test-tubes with test-tube covers arranged upon a stand of glass-tube and silver wire. These were put into the hot box and heated to 300 deg. Fahr., and then, some milk having been received from the cow into a vessel purified previously by means of this pipette attached to a syringe, the pipette having been purified, milk was drawn up into the pipette, and then, by means of the syringe, each little cap being in succession raised, a few minims of milk were introduced into each of the glasses, the caps being immediately reapplied. The result was, every one of the milks underwent fermentations, every one of them; and every one of them contained organisms, some of them as many as three different ones. The great majority of those twelve glasses which I used presented little orange specks, such as were never seen, I suppose, in any milk before; and, on examining these, I found them to be little organisms, to which I have ventured to give the name *granuligera*, because they consist of granules, different from bacteria in this respect, that you might suppose them not to be organisms at all till you had the opportunity of seeing them undergoing multiplication by fissiparous development, multiplied by crosswise fissiparous development; in a manner, however, differing from the transverse fissiparous multiplication of bacteria, in being crucial. But, besides the *granuligera*, there were bacteria of different sorts, and also some *torulæ*, but there was no *bacterium lactis*, and there was no lactic acid fermentation. What inference were we to draw? Was I to suppose that, although the lactic acid fermentation had been excluded, it was impossible to exclude others; that others were present in the milk as it existed in the cow's udder; or was it that I had not been sufficiently careful? The latter was the view I was disposed to take. The experiment had been performed in the cow-house, where certainly the air might be supposed to be reeking with organisms. I, therefore, performed the experiment a second time, and this time in the open air. It must be confessed it was not far from the cow-house, and it was a fine day at the very time of the year in which organisms most abound. On this occasion, I had twenty-four of the little glasses which you see before you. This time, again, every glass had organisms in it. At the same time, every glass seems to be different from all the rest. Such fermentations as there are here, I venture to say were never seen anywhere before. I have brought before you a diagram, showing some of them on a large scale. I want particularly to direct your attention to these strange scarlet spots which occurred in almost all of them. They began in tiny scarlet dots, which spread as fermentative changes, and, therefore, capable of self-multiplication in the substance of the milk. Here is one that is green, and here is another of an orange yellow colour. Here are two that have two kinds of filamentous fungi. I have not examined the species, but I shall very likely find that it is some species that has not been described. I found in the first experiment, as one of the organisms, a filamentous fungus of the most exquisite delicacy, though in general type of the same sort of arrangement as the common blue mould or the *oidium lactis*. The size of the filaments was so exceedingly small that twenty of them would lie abreast in a single human red corpuscle; they were smaller than even the *bacterium lactis*, smaller than the majority of bacteria. I believe no such exquisitely delicate filamentous fungus has ever been seen, even by Professor Bentley.

Now, how are we to explain this strange result? I am still disposed to believe that these organisms have got in for want of sufficient care on my part. But how are we to explain these strange appearances? Simply thus. If the *bacterium lactis* had been here, it would have taken the precedence of all other organisms in its development and the changes which it would have introduced would have made the milk an unfit soil for these organisms. Therefore I said—perhaps you might think me rash in saying so—there never were such fermentations or such organisms seen before in milk, simply because they never had the chance that they had here of coming forward; they would have been smothered—killed—by the effects of the *bacterium lactis* and other bacteria. Well, I determined to make one more attempt. This time I took the original twelve glasses. I mentioned that a large proportion of these glasses had scarlet spots, but I have not yet investigated upon what organism they depend. In the former experiment in the cowhouse, the great majority had orange spots, and those, as we have seen, were composed of heaps of granules. It occurred to me

that one cause of failure might be this. Suppose one single group of these granules to exist, and to become disturbed and broken up, it might vitiate the whole specimen of milk; therefore, instead of drawing up the milk into the pipette with a syringe and then expelling it, I determined to have it introduced as directly as possible into the little glasses. These glass vessels having been purified by heat, the piece of India-rubber connecting them could not be purified by a very high temperature; it was purified by boiling. Cotton caps were tied over the ends of the glasses during the heating. The cow was taken out again into the open air, and this day the elements were in my favour. It had been a drizzly morning, and I might fairly hope that some of the multitudes of organisms existing in the little orchard might have been washed down and that the air might have been purified. I was also more careful in this respect. I got the dairy-woman to milk the cow without drawing the hand over the teat, so that the end of the teat should always be exposed by an action of the fingers in succession. Her hands were washed with water, and the cow's udder also, and she having squirted a little milk to wash away the organisms from the orifice of the duct, the cap was removed and the end of the tube was held in the immediate vicinity of the teat; a few drachms were introduced, then the cap was readjusted, and then these little glasses were filled by the simple expedient of alternately relaxing and compressing with the finger and thumb on the caoutchouc, so that there was as little disturbance as possible of the organisms that might be supposed to be introduced in spite of my care. It is six weeks since this was done. At first sight, you might suppose, contrasting these appearances with those of the other tubes which were only filled three days earlier, that the latter milks were all pure. The truth is, all but two have organisms in them; but I may mention that all but four had obviously organisms in them before I went for my trip on the Continent three weeks ago. In the course of the three weeks that have elapsed, two others have gone; but they already showed organisms which, though very pale and insignificant, were quite easily seen by a magnifier in such considerable mass that I felt sure they must have already been growing for a considerable time; and, therefore, in all probability those that still seemed to the naked eye and to the magnifier free from organisms were really so. Accordingly, two days ago I drew out milk from one of those that seemed to be still pure, and I had the great satisfaction of finding the milk not only perfectly fluid and tasting perfectly sweet, with a perfectly normal reaction, purpling both the blue litmus paper and the red litmus paper—the normal reaction of perfectly fresh milk—but under the microscope I could not discover any organism of any kind whatsoever. Therefore, I think we are justified in saying that in unboiled milk as in boiled milk, provided, of course, the cow be healthy, there does not exist any constituent having any power of giving rise to organisms or producing the lactic or any other fermentative change.

This, gentlemen, is the first step; the second will not occupy us so long; and I must beg that you will give me the opportunity of mentioning it, because, I believe, you will agree with me that it is the far more important step of the two.

The second part of the investigation was to find absolute evidence, if possible, whether the bacterium lactis was or was not the cause of the lactic fermentation. It occurred to me that, if we could estimate with some degree of accuracy the number of bacteria present in a given quantity of the liquid, and then if we were to dilute the milk with a proportionate quantity of boiled water, we might have the diluted milk so arranged that every drop with which we should inoculate boiled milk might contain, on the average, one bacterium; and if we should do so, as it would be practically certain that they would not be distributed with absolute uniformity, we should expect that we might have as the result of these various inoculations, some glasses with the lactic fermentation, some glasses without it, some with the bacterium lactis, and some without it; and, if it should turn out that we should get those glasses with the bacterium lactis which underwent fermentation, and, on the other hand, those glasses which had no fermentation free from the bacterium lactis, that would prove the point, as, I think you will agree with me, it did, when we come to discuss the matter at a little more length after we have all our facts. Well, how are we to determine the number of bacteria existing in the liquid? This was done in a simple manner; a little covering glass, just half an inch in diameter, was used. Of course, we know how many square thousandths of an inch there are in the area of this little glass. We also know by the micrometer how many thousandths we have across our microscope, and, therefore, by calculation we know how many square thousandths there are in our field, and thus we can tell how many fields there are in the covering glass. I also, by means of this little syringe with a graduated disc and a piston rod in the form of a screw, graduated 2-100ths of a minim, by which means you

can, with perfect precision, unit 1-100th of a minim, or 2-100ths, or any number you choose. I found that 2-100ths, or 1-50th, exactly filled the covering glass, so to speak; so that, when put down upon a glass plate, the rim of fluid round about the covering glass was not one quarter of the diameter of the field; using the highest magnifying power, so that practically it was all under the covering glass. I knew, therefore, that there was 1-50th of a minim under the covering glass. If, then, I counted how many bacteria there were in a field, and took the number of the different fields and struck the average, I found how many bacteria there were on the average in the field; therefore, by calculation, how many there were under the covering glass, and how many there were in the 1-50th of a minim; and, consequently, I knew how much boiled water I ought to add in order that the drop of whatever size I might wish it to be should contain, on the average, one bacterium, and one only. This being done with a particular specimen of souring milk, I found that it was needful to add no less than one million parts of boiled water to the milk to ensure that there should be rather less than one bacterium, on the average, to every drop. Then with these inoculating drops I inoculated five glasses of boiled milk; and the result was that out of the five only one curdled; but one did curdle, and that one had the bacterium lactis in abundance; the others did not curdle, underwent no fermentation whatsoever, and had no bacteria in them. You may say, perhaps, "How was it that there were none of these different things that you have been showing us?" Simply for this reason, that although these existed, and one of them existed probably in every two or three minims of the milk, yet they were in exceedingly small proportion to the bacterium lactis, so that you might have searched, perhaps, for a whole day, with a high power of the microscope, and never discovered one. We are apt to forget how difficult it is to find these minute objects; unless they are very numerous indeed, in liquids. Therefore, when we came to dilute the milk with a million parts of water, the chances of getting anything but the bacterium lactis were exceedingly small. It was with reference to the bacterium lactis that the dilution had been made, and not with reference to these other organisms so exceedingly small in quantity. It so happened that we saw in the souring milk that there was another kind of bacterium, a moving kind different from the bacterium lactis; it was in every field, but not nearly so numerous as the bacterium lactis; it did not, however, exist in the one milk that curdled.

Now, having the bacterial ferment pure, we had the opportunity of performing other experiments; and the last experiment that I shall mention is this. These five specimens which you see before you were inoculated each with a drop calculated to contain two bacteria; these other five were inoculated each with a drop calculated to contain one bacterium; these five open glasses were also inoculated with drops each calculated to contain one bacterium; and one with a drop calculated to contain four bacteria. The result was that the specimen with the drop calculated to contain four bacteria curdled in a few days; and all these five calculated to have two bacteria to a drop curdled in a few days. The milk, you see, is perfectly solid, and curdled and soured. You will observe that no other change has taken place except the lactic fermentation, no odium lactis, and no other alteration; it is as pure in whiteness as when it was first coagulated. I may here mention that, although all these coagulated, they did not all coagulate at the same time. There was a time in the twenty-four hours during which the coagulation went on, in which I hoped that some of them were going to be permanently fluid; implying, as you would expect, that the particles of the ferment were not uniformly distributed; some had more than others, though each happened to have one. But, of the five glasses calculated to have one bacterium to each inoculating drop, three have remained fluid, and two of these others; so that, of the ten, exactly five, it so happens, have remained fluid without any curdling. I may consider myself somewhat fortunate that I have succeeded in bringing these all the way from Edinburgh in this condition. I will now deprive this of the protection in which it has hitherto lived. [Professor Lister poured out some of the milk and drank it.] It is perfectly sweet. It has a slight flavour of suet, which M. Pasteur has described as resulting from the oxidation of the oleaginous material of the milk.

Let me note this curious circumstance, that, of those specimens which did coagulate, those in the tubes coagulated considerably earlier than those in the more open vessels. At first, it seemed as if, for some strange reason, they were going to remain more fluid than those in the open vessels—even those that had, according to the calculation, four bacteria to the drop. I believe this is to be explained on the same principle as Pasteur has explained a corresponding fact with regard to the yeast-plant. He has shown that, if a saccharine solution be put in a very thin layer in an open vessel of yeast, the yeast-plant develops

to a very great extent, but very little fermentation occurs; on the contrary, if it be put into a deep vessel, the development of the yeast-plant does not go on so rapidly, but more fermentation occurs. He explains it this way: that the yeast-plant requires oxygen for its nutrition; if it get it easily, as it does in a shallow vessel in the air, it produces comparatively little effect in breaking up the sugar into its constituents. So here, in the deep vessel, the carbonic acid accumulates, supposing any to exist, as in a well. Here the bacterium lactis had but little opportunity for getting oxygen. Accordingly here, just as in M. Pasteur's experiments with the sugar, the lactic ferment produced more rapidly its effect of lactic fermentation.

But this, you say, is assuming that bacterium lactis is the ferment. Now we are coming to that point. I say that this fact demonstrates, as I believe, that the bacterium lactis is the cause of the lactic fermentation. I must add one point by way of fact. For the satisfaction of others rather than for my own, I went through the laborious process of investigating portions of all these vessels, and I found that, in every one in which the lactic acid fermentation had taken place, where there was curdling and souring, the bacterium lactis was present; and in no instance in which there was no lactic fermentation was any bacterium of any sort to be discovered. I believe that demonstrates that the bacterium lactis is the cause of this very special lactic fermentation. But, let us assume for a moment that there did exist some other particles besides bacterium lactis in the milk capable of causing a fermentation; that the lactic ferment were not the bacterium at all, but some chemical ferment. First of all, you will please to observe that we have from this experiment absolute evidence that the ferment, of whatever nature, is not in solution, but in the form of suspended insoluble particles. If the ferment had been in solution, every drop would have produced the same effect. The fact that some drops were destitute of the ferment proves that that ferment was not in a state of solution. That is absolutely demonstrated. Now, suppose we admit, for the sake of argument, that the lactic acid ferment was some non-living substance, capable of self-multiplication as rapidly as the bacterium, but not living; a strange hypothesis, no doubt—but suppose we admit it. Suppose we admit that these chemical ferments, the chemical lactic ferment and the bacterium lactis, were merely accidental concomitants of each other, it would be absolutely inconceivable that these two accidentally present things should be present in exactly the same number. But, suppose you admitted that—that there were exactly as many of the bacterium lactis as there were of the ferment, the true fermentative particles—suppose you admitted that inconceivable thing, I say it would be again inconceivable that they should accompany one another in pairs, that invariably where there was bacterium lactis there should be a ferment particle, and where there was no bacterium lactis no ferment particle. That would be as inconceivable as the other. Therefore, we have two inconceivables, one of which would have been sufficient to show that we cannot admit any other hypothesis than that bacterium lactis is the cause of the lactic acid fermentation.

But the experiment tends to even more than this. Where we find the effect so exactly proportioned, as regards the number of glasses affected with fermentation, to the adult bacteria that we count, we are led to infer that this particular bacterium, at all events, has not any spores—that there are no spores existing in addition to the bacteria. People seem often to assume that these bacteria must necessarily have spores or germs. It seems to me an unlikely thing that they should. If they are, as it were, a generative apparatus *per se*, they are constantly multiplying; why should they have spores? I do not say that bacteria may not have spores. There are very different kinds of bacteria; some may have spores, and some may not; but this sort of result seems to indicate that this particular bacterium has no spores; because, if we had, besides the bacteria that we can count, spores of bacteria disseminated through the liquid also, we should have the effect more than in proportion to those bacteria that we have. The only fallacy here is that it may be that the bacterium has not been diffused uniformly through the milk. Therefore, I do not say that in this case it is absolutely proved yet. At all events, this experiment gives us a line of inquiry, by means of which we may probably settle that point with regard to any individual case of bacterium. This, however, I do not desire to urge upon you; but, what I do venture to urge upon you, is that you will seriously ponder over the facts which I have had the honour of bringing before you to-day; and, if you do so, I believe you will agree with me that we have absolute evidence that the bacterium lactis is the cause of this lactic acid fermentation. And thus I venture to believe that we have taken one sure step in the way of removing this important but most difficult question from the region of vague speculation and loose statement into the domain of precise and definite knowledge.

ON HÆMORRHAGE FROM THE RETROFLECTED UTERUS, AND ITS TREATMENT.*

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AT the risk of being thought to occupy your time on a subject already worked out, and again to tread over well-trodden ground, I have ventured to bring up a subject which is very clinical; and one which, though apparently well discussed both for and against, has not yet been decided, at least by many, so as to be to them a rule for practice.

When discussions on the treatment of the retroflected uterus have taken place, it has generally happened that two opposite opinions have declared themselves: one strongly in favour of mechanical treatment; the other, if not actually repudiating it, yet considering it the *dernier ressort*, not to be tried till constitutional management and local treatment have failed. Between these two extremes, there are various shades of opinions, inclining to the one or the other according as experience, education, and other circumstances have affected the possessor. I shall perhaps be not far wrong when I rank the majority of the profession as forming the intermediate class.

The difference of the extreme opinions appears to me to be owing to these facts.

1. Women are not unfrequently found with completely retroflected uterus, without the least uneasiness or complaint, all their lives.

2. Women complaining of certain symptoms, and even crippled by them, are found to have retroflected uterus; all of these symptoms subsiding upon the restoration of the uterus to its normal position.

3. It is often observed that, before the retroflexion is confirmed, the uterus sometimes is retroflected, and at another time in normal position.

4. That temporary engorgement of a retroflected uterus, which had before given no trouble, frequently subsides under horizontal posture and appropriate treatment.

According as these conditions have presented themselves, in respect of number and intensity, to the various observers, so have their opinions inclined in one direction or another.

It is not my intention, nor is it suitable at the present time, to occupy this meeting with a full discussion on retroversion and retroflexion; but there is one clinical state of it, by no means unfrequent, upon the treatment of which as much difference of opinion has existed, and in a measure still exists, as on any part of the subject. Upon this subject I am desirous of adding the result of my experience. Hæmorrhages may occur from the retroflected uterus in various degrees; the remarks I shall make apply to all of them, more or less, but it may be well to take a typical example.

The uterus is completely retroflected, the body two or three times the normal size; sensitive to the touch, especially at the fundus; the os and cervix are large and patent; there are much leucorrhœa and menorrhagia, with greater or less bleedings between; coagula passing often, sometimes with pain; pain in the back, bearing down; uneasiness in the groin; and indeed all the direct and reflex symptoms produced by retroflexion exaggerated.

It has been contended that in this state it is inadvisable to handle the uterus, so as to cause its restoration to its normal position, and to retain it by vaginal pessaries. It has been argued that this state is inflammatory, and that the disturbance will increase it: that the proper thing is to subdue the inflammation, first, by depletives locally and by postural treatment, and then to replace the organ, should it not have recovered its position by the rest.

This line would be doubtless correct, were the premises upon which it rests correct also. Let us consider for a few moments these data. The effects of retroflexion of the uterus have been well recognised, and may be divided into those which are derived, first, from the obstruction produced by the flexion; and secondly, from the dependent position of the fundus. By both of these the secretions are retained beyond their usual time, a certain amount of irritation is set up, which increases the secretion, and this accumulating, distends the cavity; and thus, in the case of hæmorrhage, a larger amount is permitted to flow. Besides this, a clot, often forming, has to be expelled by uterine contractions, which cause pain, bearing down, and backache; these clots, by breaking up, by a species of decomposition, set up increased irritation and flow of blood and serum, etc. Besides this, the level of the fundus being three to four inches lower than normal, there is a greater pres-

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