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ON LATENT INFECTION AND SUBINFECTION, AND ON THE ETIOLOGY OF HEMOCHROMATOSIS AND PERNICIOUS ANEMIA.*

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(Concluded from p. 1514.)

ON THE PRESENCE OF BACTERIA IN NORMAL TISSUES.

Similar considerations and similar criticisms may be brought to bear on the observations which have been made with regard to the existence of bacteria in the normal tissues. Time and again observers, like Hauser,[35] Neisser,[36] and yet others, have found the tissues of healthy animals so frequently sterile that the occasional gaining of cultures from the organs has been by them referred to contamination in the admittedly difficult task of removal of organs or parts of organs from the body into sterile receptacles. Thus, for example, Neisser, out of some thirty-seven rabbits, mice and guinea-pigs, which he fed with various pathogenic and non-pathogenic organisms and in certain of which he further set up grave intestinal irritation by giving at the same time croton-oil or powdered glass, failed to gain cultures from growths in the liver, spleen, kidneys, lungs, etc., in twenty-four, and only gained cultures, and these in not all the organs, in the remaining thirteen. His method was apparently most complete; the animals were skinned and then placed in sublimate solution so as to sterilize the surface, then fastened out on sterile boards, the operator himself having his hands sterilized, and each organ was removed in turn by a separate set of sterile instruments and then placed in sterile vessels and melted gelatin or, rarely, melted agar poured over them, while only after two days were they examined.

The results seem most positive, and what is remarkable is that even when cultures did grow in the organs, in general they were not the forms with which the animals had been fed.

Recently Dr. A. G. Nicholls and Dr. Ford, Fellow in pathology at McGill, have been repeating these observations, and they have gained very different results and Ford has discovered wherein Neisser has been led astray. The animals employed by him so far have been rabbits, and he has taken precautions similar to those employed by Neisser to guard against contamination. Immediately after removal of the kidney or portion of the liver with sterile instruments, it has been placed in the flame of a large Bunsen burner and turned around until the surface began to "splutter," if I may so express it, thereby making sure that there should be no surface contamination. The organ or part has then been dropped into a sterilized bottle of special construction, containing melted glycerin or melted agar, so that if there were any subsequent contamination by the air it would first of all show itself on the surface of this medium when solidified. Dr. Ford will publish his whole series of observations later, but he has done sufficient to allow me to state that where organs are placed in gelatin and kept in the cold, a large portion remain absolutely sterile and show no growth, whereas when placed in agar and kept at the body temperature, the majority of livers and kidneys show relatively abundant growth after two days or less.

Here, again, I take it, the bactericidal influence of the body tissues come in. If may be that if the organs be not immediately removed after death, such bacteria as are present undergo attenuation and destruction with fair rapidity, unless, as in cases of disease, they be present in relatively large numbers, while at the same time the bactericidal powers of the tissues are depressed. What appears more evident, though, from Dr. Ford's results, is that this inhibitory action of the body tissues upon microbes that are accustomed to live at the body temperature is favored by keeping cool, or more correctly that the activity of growth of the bacteria is depressed. That Dr. Ford's results can not be ascribed to contamination is rendered evident by the fact that where he has found micrococci growing in the normal removed liver, he has found them also growing in the kidney. If certain forms of bacteria be present in one organ, the tendency for them is to be also present in the other; though it should be added that—as might be expected if these have been brought to the organs from the intestines—colon-like forms predominate, and again not infrequently more than one form is present.

Let me, before proceeding farther, gather up and group together the conclusions which may be legitimately adduced from the facts so far brought forward. They are, it seems to me, the following:

1. Normally there is a passage out of leucocytes through the mucosa on to the free surface of, more especially, the alimentary tract.

2. These leucocytes, while in part undergoing a destruction, in part find their way back between the epithelial cells, bearing with them foodstuffs and solid particles, among which may be the bacteria present in the cavity of the gut.

3. During the active congestion which accompanies digestion, the passage out and return of these wandering cells is increased.

4. These cells upon their return find their way either into the lymphatic channels or the venules of the portal system.

5. In either position, they tend to be destroyed and digested by the leucocytes and thus, while preparations of the mesentery and of the mesenteric lymphatic glands may show abundant bacteria, the vast majority of these at the same time show obvious degeneration, while cultures made from the mesentery or from the lymphatic glands upon ordinary media by ordinary methods as a consequence tend to remain sterile. Similarly, in the normal liver, the same rapid destruction takes place, so that here again, by ordinary methods, no evidence of living bacteria is obtainable.

6. By the employment of adequate methods it can be demonstrated that even in the healthy liver and kidney in a large number of cases, in one animal at least—the rabbit—a certain number of living microbes are present at any one moment so that, if the healthy organ be removed from the body, cultures can be obtained of these living microbes.

7. It is most probable, further, that in ordinary health a certain number of bacteria which have not been destroyed by the leucocytes or removed by the lymphatic glands or endothelium of the portal system, pass either through the thoracic duct or through the liver into the systemic blood. Such bacteria tend to be removed more especially by the kidneys, though it may be by other glandular organs. In any case the ordinary methods at present employed in making cultures from blood are inadequate to detect the presence of such bacteria unless they are of such a nature or are circulating in such quantities that the whole number is not destroyed by the bactericidal action of the shed blood.

LATENT INFECTION.

It follows further, from these conclusions, that there

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does exist a condition of what the French term "latent microbism," or what I think should be more correctly termed, for my present purposes, "latent infection." We have abundant evidence that even in the healthy feces such forms as the pyococci, streptococci and the bacillus pyocyaneus are to be encountered fairly often. We further know that the commonest form inhabiting the intestine, that which outgrows all other forms, namely the colon bacillus, even when obtained from perfectly healthy feces, may show marked pathogenetic properties when inoculated into the lower animals.

We also know as a common fact in pathology, that just as one swallow does not make a summer so an isolated microbe gaining entrance into the system, does not usually set up disease. Save when we are dealing with the most virulent forms of pathogenetic micro-organisms and with animals which are peculiarly susceptible, it requires numerous bacteria entering at the same time to so lower the resisting powers of the tissues as to there survive and proliferate. Even with the tubercle bacillus it has been calculated that, in the very susceptible rabbit, at least from twenty to thirty have to be inoculated subcutaneously before the disease can surely be set up; any lesser number is destroyed. If, therefore, in the intestine, here and there at scattered points, individual bacteria are being introduced into the system from time to time, that does not necessitate proliferation and consequent infection; we can easily understand that if the tissues there possess their normal powers, isolated bacteria tend to be destroyed by the cells or the containing leucocytes at the immediate point of entry; and, as a matter of fact, study of the mesenteric glands and the difficulty in obtaining cultures from these, even when sections of the same show relatively abundant bacteria, is clear evidence that this is the case.

ON CERTAIN CASES OF SURGICAL INFECTION.

Only the other evening I was talking over these matters with my colleague, Dr. Armstrong, surgeon to the Montreal General Hospital, and he put to me certain very pertinent questions. "Why," said he, "do we surgeons dread operating upon the robust city man apparently full of health and vigor, who wants to rush in upon us on the Friday or even upon the Saturday afternoon, to have some such small operation performed upon him as, for example, the removal of hemorrhoids, in order that he may be back again at his business on the Monday morning? Why is it that the chances are so greatly against such operation being safe? Why, on the other hand, if we coop up that man for two or three days previously and thoroughly purge him, is the operation a trifle, and we can be practically sure that there will be no complications? The sudden change in his diet and habits can scarce improve the vitality and resisting power of his cells. Why, again, is it our common experience that our best cases, upon which we can operate with the certainty of gaining good results, are those who have been almost bedridden with chronic disease and have been in a condition of invalidism for long months and living upon a restricted diet? Why, again, do we fear to operate upon cases suffering from chronic constipation? Can any more satisfactory explanation of these facts be given than this theory of latent infection and of the possible infection of wounds, not from outside or from the skin, but from bacteria circulating in the tissues, which, under normal conditions, are destroyed and rendered harmless, but which under the abnormal traumatic conditions of the operation are now able to proliferate and set up local disturbances?"

TERMINAL INFECTION.

But, in addition, we can equally well understand that if from some cause or other, as for example, from inflammation along the intestinal tract, whereby excessive numbers of bacteria are introduced, or again in conditions such as are afforded toward the conclusion of long-continued chronic wasting disease, in which the reactive powers of the tissues are greatly lowered, or again where there is temporary lowering of the vitality by injury or operation, then everything favors the multiplication of bacteria so introduced and the development of either localized—so-called cryptogenetic infection—or of general septicemic disturbance.

The admirable and, I would say, classic observations of Flexner,[37] on terminal infections, show in the most vivid light how common it is to have death preceded by such general or local infection by germs totally foreign to the main morbid condition, and amply confirm Osler's[38] well-known remark that "persons rarely die of the disease with which they suffer."

POST-MORTEM INFECTION.

If we accept the conclusions above mentioned, we gain a more correct understanding of what I may term "post-mortem infection" of the body. The usual explanation of the abundant growth of bacteria in the various organs after death is that while there may oftentimes occur an agonal invasion of bacteria, the essential cause of such infection and subsequent putrefaction is the entry of bacteria, more especially through the intestines after death. Birch-Hirschfeld[39] has lately reaffirmed this, and has brought forward certain observations of his own in favor of such a conclusion. While he admits that the agonal invasion may occur even in the absence of demonstrable lesions of the epithelial layer, he concludes that a post-mortem invasion of the internal organs by intestinal bacteria is a constant phenomenon, occurring in the majority of cases about ten hours after death, with especial frequency in the liver, but also met with in the kidneys, spleen, portal and heart blood and bile. It is an interesting point that Birch-Hirschfeld, in this supposed invasion, admits that the various organs show no constant sequence of infection, as again that morbid changes in the intestine have no influence on the time of the appearance of the bacillus coli in the internal organs. It is most interesting to further observe that this period of ten hours mentioned by him corresponds singularly with the maximum period, mentioned by Flexner, at which the blood of the cadaver was found to lose its bactericidal power; and lastly, it is of importance to notice that those who have explained post-mortem infection by this method have never demonstrated, what ought, according to this view, to be most clearly demonstrable, namely, the existence of masses of bacteria in special abundance in the intestinal wall and appearing to be growing through that wall into the blood-vessels and surrounding tissues.

It is impossible from the above observations that I have recorded to come to any other conclusion than that at the moment of death, or shortly before, the lowering of the vitality of the tissues permits a larger number of bacteria than normal to be present in the living state in the blood and lymph. Just as when one removes the blood or takes the tissue juices outside the body and adds to certain quantities of these fluids a fair number of bacteria, the tendency is for certain of those bacteria to be destroyed during the first few hours, then gradually for the remainder to multiply; so in the dead body, after death there would seem to be often, but not always, a

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preliminary period in which the bactericidal action of the tissues continues and the number of bacteria to be obtained from the tissues by ordinary methods is singularly small: following this there is multiplication. In short, our ordinary methods are imperfect, inasmuch as they only give us results when bacteria are present in relative abundance. As a consequence, it is possible for us, fortunately, often to determine what is the main invading microbe, but even with them, as shown by Flexner's results, the greater the care that is taken, the greater the variety of bacteria which may be found in the body after death.

SUBINFECTION.

But apart from this latent infection and the sudden and acute one to which it may at times give rise, if we admit this normal passage in, and normal destruction of, bacteria by the tissues, there is possible, it seems to me, an intermediate condition which I would term "subinfection," a condition in which, as a consequence of chronic inflammatory disturbance in connection with the gastro-intestinal tract, there may for long periods pass in, through the walls of the stomach or of the intestine, a greater number of ordinary bacteria inhabiting the tract, and, while the bacteria undergo the normal and inevitable destruction by the cells of the lymph glands, the liver, the kidney and other organs, nevertheless, the excessive action of these cells and the effect on them of the bacterial toxins, liberated in the process of destruction, may eventually lead to grave changes in these cells and in the organs of which they are part—changes of a chronic nature. At no individual moment may we find evidence of the presence of large numbers of living bacteria in such organs, but we may find the evidence of their presence in the cells, and may find certain chronic inflammations associated with, or the result of, this overwork of the bacteria-destroying cells. It is possible, I would urge, that there may exist a morbid condition, the existence of which has not so far, to the best of my knowledge, been fully recognized. We must, I think, admit the existence of the following forms of infection:

1. *Fulminating Infection*—In which, from the onset to the conclusion, the tissues are unable to overcome the virus.

2. *Acute Infection*—In which, while at first the bacteria gain the upper hand, the tendency is for the tissues to be stimulated eventually to counteract the germs and their toxins.

3. *Chronic Infection*—In which the tissues have not the power of wholly destroying the bacteria, although they may arrest their activity, and thus the bacteria constantly but slowly gain the advantage.

4. *Subinfection*—In which the tissues readily destroy the invading bacteria, but in which, just as water constantly dropping makes a hole in the stone, eventually, with recurrent invasion, the tissues become worn out, whereupon chronic or acute infection may supervene.

The absolute recognition and determination of this last condition is rendered peculiarly difficult by the fact that any chronic catarrhal or inflammatory condition of the intestines is accompanied by abnormal fermentative changes therein. And thus at the present time it is almost impossible to distinguish and divide conditions which might be due to this combined cell exhaustion and cell intoxication from the intoxication and the disturbances due to increased absorption of soluble poisonous products through the intestinal wall.

Yet certain observations that I have been making during the last two years do, I must confess, lead me to believe in the existence of such a condition of subinfection. In the first place I found these minute diplococcoid bodies peculiarly frequent in the liver cells in cases of hepatic cirrhosis, and since finding these, the more I have myself made autopsies in cases of this condition, and the more I have carefully studied the records of others, the more it has been brought home to me that accompanying ordinary progressive cirrhosis there is a chronic catarrhal condition of the intestines, together with a definite enlargement of the retroperitoneal and mesenteric lymphatic glands. Here it is more especially in the cells at the periphery of the lobule that this presence of these bodies is noticeable, in those cells, that is to say, which are first fed from the blood coming from the portal vessels, and which are again most liable to undergo atrophy and to be affected by the fibroid change occurring in the interstitial tissues.

My first view that these little bodies either taking on a slight or an intensive stain, or seen purely as fine double pigment granules, were directly associated with cirrhosis and indicated a specific micro-organism, was rapidly modified by the discovery that cultures from the cirrhotic livers and from the bile in such cases, while at first tending to give a form of diplococcus, upon subseculture and passage through animals, developed into a form morphologically unrecognizable from the colon bacillus, while frequently absolutely typical colon bacilli were obtained from these organs and from the rest of the body.

But while this is the case, the frequency with which the colon bacillus has been found by other observers, associated with more acute hepatic disease, and with which, in one form—the so-called hypertrophic cirrhosis—other observers have noted its presence, renders it not impossible that this bacillus may have some part to play in connection with the condition.

HEMOCHROMATOSIS.

Recently there came to us a case of well-marked hepatic cirrhosis associated with great pigmentation of the skin and the intense development of the condition known as hemochromatosis. In this, as in other cases of hemochromatosis, there was iron-containing pigment in the liver, the mesenteric glands, the pancreas, and to a less extent in the spleen, kidneys and the heart. What is the cause of this hemochromatosis has been a matter of very considerable conjecture of late years. There is a very full paper on the subject in the last issue of the *Journal of Experimental Medicine*, by Dr. Opie, of Baltimore, a paper so full and thorough that here I need not go into the various theories that have been adduced; I will only say that Dr. Opie comes to the conclusion that the condition is a distinct morbid entity characterized by the wide-spread deposition of the iron-containing pigment in certain cells, and the association of iron-free pigment in a variety of localities in which pigment is found in moderate amount under physiologic conditions. With the pigment accumulation there is degeneration and death of the containing cells, and consequent interstitial inflammation, notably of the liver and pancreas, which become the seat of inflammatory changes accompanied by hypertrophy, while, when the chronic interstitial pancreatitis has reached a certain grade of intensity, atrophy and diabetes ensue, and this last is the terminal event in the disease.

Dr. Maude Abbott, who has been working in my laboratory, on this subject, for some months, has reached somewhat different conclusions. She called my attention to the fact that where there is marked destruction of the blood the spleen may also be the seat of pigmentation,

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whereas in the diabetic and cirrhotic cases, as again in pernicious anemia, the spleen is not implicated. Examining some of these typical cases of hemochromatosis she reported to me that in some instances, she noted frequent diplococcoid bodies. To a slight extent the deposit of iron-containing pigment is present in a large number of cirrhotic livers which she has examined, and she has been especially struck by the fact that one and all have shown either marked inflammatory disturbance in cases in which such occurs unassociated with cirrhosis, it also occurs in cases unassociated with cirrhosis either of the liver or pancreas. Examining the records of the connection with the intestines or some chronic suppuration elsewhere in the body—conditions in short leading to more or less chronic destruction of the blood. When now I come to study her material more fully, and with the highest power, to my astonishment I find that where this pigment has not clumped together into too large masses, in the liver cells for example, as again in the abdominal lymphatic glands, there are, in a very large proportion of the ultimate fine masses of pigment, reacting to Perl's test and containing iron, distinct diplococcoid forms or bodies. Of this there can be no doubt. In short, the condition of hemochromatosis is of bacterial origin and, just as Hintze,[40] and before him, von Recklinghausen,[41] pointed out that the slightest case of hemochromatosis presents itself merely a brownish coloration of the intestinal walls, so here we may have a succession of cases in which at first only the intestinal walls and the mesenteric glands become the seat of the deposit of this pigment, and to a slight extent the liver, through cases in which the liver is involved and there is associated or accompanying cirrhosis, to cases in which the pancreas also becomes the seat of this abundant deposit of the minute pigment granules, of modified "corpses" of bacilli in the cells. I have no doubt concerning this; the diagram is a faithful reproduction of a portion of one of these livers of hemochromatosis, from a case described by Kretz,[42] which has come through several hands into that of Dr. Abbott. You will see that whereas in certain regions it is dense and it is impossible to make anything out, there are other parts in the cells where these little diplococcoid bodies definitely take on the reaction for iron.

Where we have *diabète bronzé*, or again extensive cirrhosis of the liver with hemochromatosis but without diabetes, there deposit of this iron is so extreme that certain of the cells, more especially at the periphery of the lobules, become little more than a mass of agglomerated iron-containing pigment, and what is more, this pigment is now to be found in the connective tissue at the periphery of the lobule and, as Dr. Abbott points out, and as others have also concluded, the little masses of pigment indicate the remains of liver cells. In fact, the condition is a very extreme one.

PERNICIOUS ANEMIA.

The nature of this deposit of pigment in the liver in conditions of hemochromatosis is identical with, though more extensive than, that first recognized by Quincke, and of later years more especially dwelt on by Wm. Hunter, which is found in the liver in pernicious anemia. There is the same finely granular nature, the same tendency for the pigment to be accumulated in the cells in the immediate neighborhood of the bile capillaries, and here again there is the same reaction with ammonium sulphid, and by means of Perl's test with potassium ferrocyanid. Examining a series of livers from cases of pernicious anemia, I find in them identically the same condition, namely, that whereas under the ordinary high power, or even the ordinary 1/12 oil-immersion, all that one sees is an irregular massing of fine granules in the liver cells, if one examines carefully and conscientiously by means of a yet higher power of immersion-lens, these irregular granules resolve themselves into irregular clumps of stumpy ovoids, as again of minute diplococcoids, and again into isolated diplococcoid bodies which may or may not show a fine halo round them, situated in the liver cells. Nay more, in advanced cases of pernicious anemia, one finds the same bodies also crowded in the very much swollen endothelial cells. In both positions these take on a reaction for iron, but even when stained for iron, as by Perl's test, the diplococcoid nature can be made out in a large number of the isolated masses on careful focusing.

I do not mean to say that all show themselves as diplococcoids; there are numerous isolated granules as again bodies of a more oval shape, and again certain bodies, roughly the same diameter, which often appear to be definitely bacterial in form. But on careful study the number of double bodies, of dots of the same size, is so remarkable and so frequent that the diplococcoid nature of the granules is their especial characteristic.

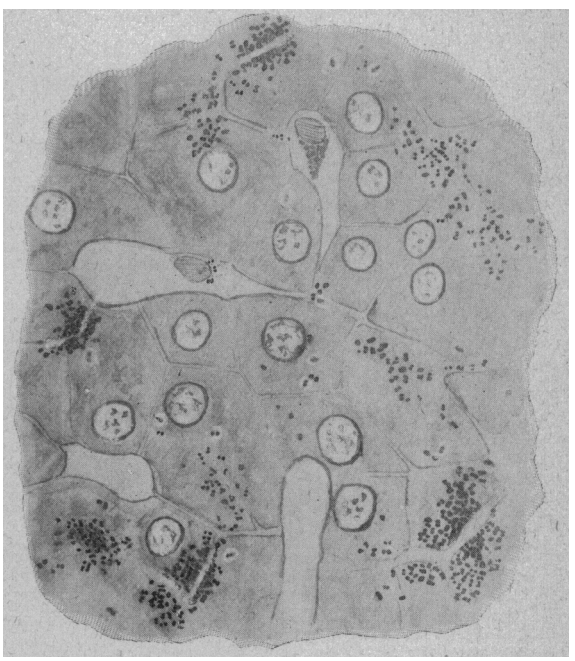

Fig. 2.—Section of liver from case of hemochromatosis (pigmental cirrhosis) stained with alum carmin, then treated with weak hydrochloric acid and later with dilute potass. ferrocyanid solution. Drawn under camera lucida, Reichert 1/18 immersion-lens, ocular 4.

It is now more than a year since my attention was called to the fact that the colon bacillus when virulent is especially liable to set up hemorrhagic inflammation in the lower animals, as again in certain cases in man, so that in hemorrhagic peritonitis we very frequently come across abundant cultures of this form. As Sidney Martin has pointed out, parallel inoculations in lower animals, of the closely allied typhoid bacillus, lead to a non-hemorrhagic disturbance. Thinking over this it occurred to me that very possibly the toxins of the colon bacillus might have some peculiar action on the blood and on the vessels, and by following this train of thought it occurred to me that the toxic substance which Hunter concluded must become absorbed from the upper portion of the gastro-intestinal tract, to explain the pronounced destruction of red corpuscles in pernicious anemia, might possibly be of bacterial origin. The point, I believe first drawn attention to by von Jacksch, and more re-

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cently corroborated by Dr. Finley of Montreal, that in typical cases of pernicious anemia there is an absence of hydrochloric acid in the gastric juice, an observation since confirmed by other observers, seemed again to render the abnormal multiplication of bacteria within the stomach extremely probable. With this end in view I suggested to one of my demonstrators, Dr. D. Anderson, that he make a special study of the bacteriology of the stomach in cases of pernicious anemia. This disease is not very frequent, and it is difficult to accumulate any large number of cases, but during the year, Dr. Anderson has studied three of these in the laboratory at the Montreal General Hospital. He has found in all a complete absence of hydrochloric acid, with the presence, however, of considerable quantities of lactic and some butyric acid, and in all three, to my great astonishment, he has obtained by plating pure cultures of the colon bacillus. This colon bacillus has been haunting me these last years, appearing to reveal itself everywhere, and I could hardly believe these results, but Dr. Anderson obtained similar ones in connection with a test-breakfast on one of the patients during life, and was absolutely convinced as regards the correctness of his results; and what is more, on making sections from one of the stomachs, he found numerous diplococcoid forms in the submucous tissue. This I should add was long before I had realized the nature of the pigment in the liver. In order to confirm the result, I asked Dr. Ford to make an independent examination of a case at the Royal Victoria Hospital, under Dr. James Stewart. He gave a test-breakfast to the patient and absolutely confirmed the findings of Dr. Anderson in every respect. In this fourth case plates made from the breakfast gave abundant and pure cultures of the colon bacillus. The form was at first a little abnormal, the colonies were of a more opaque white than usual, but later separate cultures from several colonies gave a perfectly typical form, endowed with motility, and in every respect corresponding to the tests for the colon bacillus.

Thus, then, we have in these cases of pernicious anemia in the first place some chronic inflammatory condition of the mucous membrane of the upper gastro-intestinal tract, leading often to atrophy. In the second place we have the abundant presence of the colon bacillus here in the upper intestinal tract; in the third we have Dr. Anderson's observation of the presence of the modified form of the colon bacillus within the walls of the stomach, and in the fourth, the dead unstaining forms of bacilli—these minute brownish diplococcoid bodies present in the endothelium of the liver capillaries and again heaped up in the liver cells. My own opinion on examining these specimens is that in the majority of cases the bacteria are already dead when taken up into the liver cells, and that we are dealing, as I say, with the corpses of bacteria.

There are very many points in connection with these thoroughly surprising observations which need further elucidation. I have throughout this lecture already referred so frequently to the work of those in my laboratory that I dare say no more; it would be unfair to Dr. Anderson and to Dr. Ford to prematurely publish more concerning their work. There is one point that will probably come to everyone's mind, to which I must briefly refer, that is, why do these colon bacilli in the liver cells and elsewhere in this broken-down form take on the curious brown pigmentation, and actually take up iron? Only last Saturday Dr. Ford showed to me cultures that he had made of the colon bacillus outside the body, which were becoming diplococcoid in shape and which took on this brown staining. He has been able, in short, outside the body, to reproduce both the appearance and the properties of these modified colon bacilli in the tissues. He will later describe his methods.

I am now very careful not to state that the colon bacillus is the primary or the essential cause of either cirrhosis or pernicious anemia; indeed, I think that it is probably not, that in either case there is some primary and underlying factor favoring its entrance into the economy: this, however, I do say, that a study of these conditions does confirm me in the belief that the constant destruction and taking up of excessive numbers of these, and it may be other bacteria of similar pathogenetic powers, does affect the cells and does affect their activity. These observations, therefore,, in my opinion, confirm a belief in the existence of the condition of what I have termed subinfection. Nay more, I believe that in the development of many chronic fibroid conditions, this subinfection will be found to play a definite part. "But," as Plato was wont to remark in a manner strangely and suggestively modern, "this is calculated to afford the subject-matter of another dissertation."

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Late Payment of Doctor's Bill.—The following is an extract from the will of a citizen of Mt. Pleasant, Ia., and unique from the fact that after so many years the doctor's bill has been paid. Our correspondent who furnished us the item says that it so rarely that any one pays a bill of this kind when it can be avoided, he thinks it worthy of special notice, with which our readers will agree. The extract reads:—"Bejamin Dudley, of Lexington, Ky., saved my life by a surgical operation in the year 1837, and by giving me medical attention for two months. I had nothing wherewith to pay the doctor for his services, but promised him as soon as I was able to pay him I would do so. His usual charges in such cases would be $500. I did not feel able to pay that debt for about thirty years. Since then I have neglected to pay this debt which I justly owe, with 6 per cent. interest until paid. Dr. Dudley having died it will be due his heirs."

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