temperature has become normal, and, despite their almost cruel hunger, to lead them very gradually to the ordinary diet, which is never so much desired as after recovery from typhoid fever.

THE GOULSTONIAN LECTURES

ON

THE LIFE-HISTORY OF THE MALARIA GERM OUTSIDE THE HUMAN BODY.

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LECTURE II.

DETAILS OF THE MODE OF ESCAPE OF THE PARASITE.

I HAVE endeavoured to show that the flagellated phase of the malaria parasite is, in all probability, the extra-corporeal homologue of the intra-corporeal sporulating body; that the latter provides for the propagation of the plasmodium inside the human body, whilst the former provides for its propagation outside the human body. I also dwell on the fact that it is only when the plasmodium has escaped from the body that this flagellated phase can and does appear. The question now comes to be: seeing that escape from the body of its human host is necessary for the development of this, the first phase of the extra-corporeal plasmodium, how is this escape brought about?

As already pointed out, parasites leave the bodies of their hosts, in pursuit of the interests of the species they belong to, in many ways, each species having a special habit of its own in this respect. Thus, confining ourselves to human parasites, the coccidium oviforme, the ova of the liver fluke and of some other liver parasites are carried out in the bile; the ova of bilharzia quit the body in the hæmorrhage—the hæmaturia—which their presence in the walls of the bladder provokes; the guinea-worm bores its way to the surface of the body and provides there a hole by which its young emerge; the muscle parasites, such as the cysticerci, escape by being swallowed by an animal that preys on the measly flesh; the blood parasites, filaria nocturna for example, are liberated by a suctorial insect, the mosquito, and so on.

Parasites escape from their permanent and from their intermediate hosts in one of four ways—either in virtue of their own efforts, of the efforts of the organism they are lodged in, by the assistance of some extraneous agency, or by the decomposition of the host after death.

We have seen that so long as the future extra-corporeal form of the plasmodium is inside the human body it is enclosed in a blood corpuscle from which it does not emerge, or from which it emerges only as a passive body—a motionless passive spore. It is impossible therefore for the plasmodium to escape from its host by its own efforts. Neither is there any evidence that the plasmodium is ever extruded by the efforts of its human host, in the excreta, or in a hæmorrhage. Lying in a corpuscle it is difficult to understand how it could be excreted; for blood corpuscles, though they may escape in the excreta as the result of a hæmorrhage, are never given off as excrementitious matter. Therefore, as it neither escapes in virtue of its own active efforts, nor passively in a hæmorrhage or excretion, the only way in which the plasmodium can possibly get out of the body is through the intervention of some outside agency, or on the occurrence of decomposition after the death of the human host.

I leave the latter out of consideration as being in the highest degree improbable; for malaria is far from being a fatal disease, and the plasmodium, like other parasites, is not likely to depend on what, relatively to the frequency of malarial infection, is altogether an exceedingly rare and exceptional occurrence. The method Nature elects for the liberation of any given parasite is always one that is reasonably regular and frequent in its operation. If this be so, then, in the case of the plasmodium, seeing that all through

the greater part of every malarial infection the extra-corporeal sporulating forms are being created and circulate in a potential form in the blood waiting to fulfil their function on the chance being afforded them, this method of liberation must operate during the life of the human host. We are justified, therefore, in concluding that, under ordinary natural conditions, the possibility of the occurrence of this chance must be equally constant.

THE MOSQUITO THEORY.

Casting about for an agent that would meet the requirements of the case it occurred to me, as it had already occurred to Laveran, that, as the plasmodium is a passive blood parasite, its escape from the human body might be effected on the same principle that the escape of the passive muscle parasites is effected. As the latter obtain their opportunity by being swallowed by some flesh eater—some carnivorous animal—I thought the former might get its chance of development by being swallowed by some blood eater—some suctorial animal, such as the flea, the bug, the louse, the leech, the sand fly, or the mosquito.

The geographical distribution of malaria, and other very manifest considerations, seem to point to one or other of the two last as the most likely liberating agent, and the notorious association of malaria and mosquitos with damp and stagnant water seemed to indicate more especially this insect.

ANALOGY WITH FILARIA.

I was further impressed with the probability of the mosquito being the liberating agent of the plasmodium by a consideration of the remarkable similarity that obtains between the structure, habits, and requirements of the plasmodium and the structure, habits, and requirements of the filaria—a parasite which I had already shown to be dependent on the mosquito for liberty and the opportunity for development.

Thus, in the first place, the plasmodium and the filaria are both of them blood parasites, and both of them require to leave the blood in order to continue their respective species. Again, the filaria of the blood—filaria nocturna at all events—is enclosed in a loose sheath. Similarly, the potential flagellated plasmodium, whether as sphere or crescent, while in the blood vessels is enclosed in a blood corpuscle which practically functions as a sheath. The filaria is sheathed to prevent its escaping from the blood vessels into the perivascular tissues for the reason that, did it get there, or did it escape from the blood vessels, it would be out of the way of the mosquito when this insect visited the body of the host. The filaria has a very elaborate and powerful oral armature—a piercing apparatus—which it seems always eager to use. To prevent the premature use of this weapon on the walls of the blood vessels Nature has muzzled the filaria by enclosing it in the loose sac or sheath I refer to; so long as the parasite is inside this sac it cannot apply its oral armature to the walls of the blood vessels. The plasmodium is similarly sheathed by the blood corpuscle it lies in; because, were it free in the blood, it would be set on immediately and destroyed by the phagocytes. The filaria is sheathed to prevent its committing suicide; the plasmodium is sheathed to protect it from being murdered. The sheathing in both instances has for its object the same thing—the preservation of the sheathed organism.

The sheath in which the filaria is enclosed is easily demonstrated. It is not always easy, however, to make out the enveloping corpuscle which functions as a sheath or protecting agent for the plasmodium, either in its phase of potential flagella-producing sphere or as crescent. Sometimes, however, the plasmodium may be detected in the act of slipping out of or bursting its sheathing corpuscle; at such a moment the existence of the corpuscular sheath is very apparent. In the case of the crescent plasmodium the remains of the enveloping corpuscle can generally be readily recognised in the line that, bow-like, spans the concavity of the crescent. The preparation from which the accompanying drawing (Fig. 13) was made clearly demonstrates the corpuscular nature of this bow. The drawing represents a double crescent of a peculiar type, the only one of its kind I have ever come across. As I do not recollect to have seen either a description or a drawing of the same kind of double crescent, I fancy it

must be exceedingly rare. The case from which the preparation came was one of irregular fever and malarial cachexia in which the blood contained large numbers of crescents of the usual type. You can see that there are two separate and distinct crescents lying together and so disposed that their concavities face each other, the upper horns being in apposition but the lower horns being separated by a considerable interval. You can also make out that a very delicate line unites the lower horns, and that the space between the bodies of the twin crescents is occupied by a sheet of very pale hæmoglobin. This figure affords a convincing explanation, if

Fig. 13.

such were needed, of the true nature of the arc line in the ordinary crescent. This line does not belong to the parasite, but to the blood corpuscle in which the parasite lies and had developed. Did it belong to the parasite, were it an integral part of the parasite, then, in the case of the twin crescents represented, each crescent would have its own special arc line—two crescents, two arc lines. This, you see, is not the case. The two crescents developing in the same corpuscle have been compelled to share the corpuscular capsule in common.

PHAGOCYTOSIS AND THE MALARIA PARASITE.

It is very curious and instructive to watch the behaviour of the phagocytes towards the plasmodium, and to mark how Nature, by means of this corpuscular sheathing, guards the parasite from harm from this quarter. So long as it lies inside a red blood corpuscle and the hæmoglobin and capsule of the enclosing corpuscle are moderately healthy, so long is the parasite safe from the phagocytes; but so soon as it leaves the corpuscle, as when it arrives at the mature stage of the sporulating form or when it floats about in the blood for a short space as a free spore, it becomes exceedingly liable to be swallowed and destroyed by the phagocytes. It would seem that the plasmodium at the spore stage instinctively seeks to bury itself in the blood corpuscle as much with a view to obtaining shelter from its enemy as to obtaining food. I have often watched the behaviour of the phagocytes towards the various forms of the plasmodium; and, though I have many times seen the free extra-corpuscular forms engulfed by the phagocytes, I have never seen such a thing happen to any of the forms of the intra-corpuscular parasite. This fact is strikingly brought out in the cases of the crescent and the crescent-derived forms. So long as the crescent remains a crescent it is enclosed in what may be described as the shell of a red blood corpuscle—the corpuscle in which it was developed—and so long it is safe. I have seen a phagocyte move up to one of these crescent bodies, touch it with its pseudopodia first at one point then at another, move round about it feeling, as it were, if all were right within, suspicious apparently that things were not quite as they should be. But the corpuscular capsule seemed to deceive the phagocyte; for, after a time, the vigilant watchman would leave the masked parasite and move away, satisfied apparently, to another part of the field. Should, however, the crescent proceed to development in the direction of becoming a flagellated body, to attain which stage it has to burst and leave the sheltering blood corpuscle, it is then, being now no longer protected by its corpuscular sheathing, exceedingly liable to be set on and devoured by the phagocytes. This beautiful illustration of phagocytosis and protection is often and readily witnessed in slides of malarial blood.

The activity of phagocytosis towards these developing flagellated bodies even in blood on the slide, that is, in blood outside the body, is very remarkable, and constitutes another reason for thinking that the flagellated body does not pre-exist as such in the blood, and is an additional argument for regarding the flagellated body as a purely extra-corporeal

phase of the plasmodium. Did these bodies leave the sheltering corpuscle while yet in the circulation, and where the phagocytes are particularly active, they would be immediately set on and destroyed. Therefore it is that they do not come into evidence, do not excapsulate until the blood outside the body has cooled down somewhat, and the phagocytes have become less active.

THE PLASMODIUM AND THE FILARIA BOTH CAST THEIR PROTECTING ENVELOPES.

Another parallel between the filaria and the flagella-producing forms of the plasmodium lies in the facts, that not only are both parasites provided with a sheath, but both parasites cast this protecting covering when they get outside the body, and in both this casting of their sheaths can be artificially brought about on the microscope slide.

ESCAPE OF FILARIA FROM ITS SHEATH.

To study this phenomenon in the case of the filaria we place an ordinary vaseline sealed preparation of filaria-containing blood near a window in frosty weather, or, if the weather be mild, on a block of ice. The slide is left in the cold for several hours—say, overnight—and then examined with the microscope at the ordinary temperature of the room. We shall then find that, as the slide warms up, the chilled and languid filariæ gradually resume their usual active movements. But, in addition to this, in addition to the wriggling about like a worm on a hook seen in ordinary unchilled preparations of fresh blood, the filaria begins to indulge in a peculiar rushing, butting movement of quite a new character. Lying inside its long, loose sheath, it ever and anon retires towards the tail end of this, and then suddenly and rapidly darts forward, throwing itself with great force against the head end of the sheath. Evidently this butting movement is an endeavour on the part of the parasite to break through and escape from the sheath. The chilling which the blood had been subjected to has had the effect of causing the hæmoglobin to leave the red blood corpuscles and become diffused through the liquor sanguinis. This diffusion of hæmoglobin has thickened the blood, and so favours, and perhaps has provoked, the efforts of the worm to escape. We can see that the thick and viscid blood clings to the sheath and holds it, as it were, thereby enabling the little animal within to butt the sheath more effectually. Sooner or later it succeeds in effecting what is manifestly the object of these butting movements; it breaks through the head end of the sheath, and finally wriggles itself free from the trailing encumbrance (Figs. 14, 15). And now another thing is

Fig. 14.

noticeable about the movements of the filaria. Whereas, while still in its sheath, though very active in wriggling about, the filaria never changed materially its position on the slide and there was no need to shift the slide about to keep the parasite in the field of the microscope, now, when it has succeeded in ridding itself of the sheath, the style of move-

ment undergoes a complete change; the worm is no longer stationary but begins to travel about all over the slide, moving restlessly from one part of the preparation to another as if searching for something, so that to keep it under continuous observation the slip has to be constantly shifted. The wriggling stationary movement is changed into a locomotive movement.

Fig. 15.

ESCAPE OF PLASMODIUM FROM BLOOD CORPUSCLE.

Similarly, as I have pointed out, the crescent form of the plasmodium when newly abstracted from the circulation lies motionless in its sheath—the sheltering blood corpuscle; it is stationary. But, when the crescent has been outside the body for a very little time, it commences to change its shape, and in doing so ruptures its corpuscular capsule. The parasite then—like the filaria on the chilled slide—becomes free in the blood. And just as the filaria freed from its sheath acquires a locomotive faculty and travels away, so the flagella, which develop on the disappearance of the corpuscular capsule, tend to break away and to swim to a distant part of the preparation. Both parasites on ridding themselves of their sheaths develop locomotor habits.

These may seem small and insignificant facts to dwell on. Not so; the most trifling anatomical or physiological fact has a meaning, could we but read it aright. This meaning has nearly always—particularly in the lower forms of life—a direct reference to the interests of the species exhibiting the phenomenon. I can easily interpret and demonstrate the meaning of these things which I describe about the movements of the filaria. I would seek to apply the reasoning and interpretation which holds good for the filaria to the plasmodium; to draw from the analogy of the filaria some assistance in getting at the life-history of that other blood parasite, the plasmodium.

FUNCTION OF THE SHEATH IN FILARIA.

Let us follow out the meaning of the facts in the case of the filaria. I have already pointed out the reason for its being enclosed in a sheath—to prevent its using its oral armature on the blood vessels of its human host and thereby escaping into the perivascular tissues, where it would be out of the reach of the friendly mosquito. When the mosquito has transferred the filaria, and the blood the filaria floats in, to its stomach, the filaria is still in its sheath. Presently, however, the blood in the insect's stomach undergoes exactly the same thickening from escape of hæmoglobin into the liquor sanguinis which we produced artificially on our chilled slides. Thus, in the mosquito, the filaria is provided with the physical conditions which prompt it to try, and which are necessary for enabling it to break through its sheath; and this in time it succeeds in doing (Fig. 16). But when it has got through its sheath it is still relatively a long way from its destination—from the end of its journey. The filaria has to get into the thoracic muscles of the mosquito before it can utilise this insect as an intermediate host in which to complete its metamorphosis, a metamorphosis effected in

the thorax and not in the abdomen. It has to traverse from the centre, perhaps, of the mass of blood in the mosquito's stomach to the walls of the stomach, and thence to the thoracic muscles (Fig. 17); a long journey, if we bear in mind the size and equipment of the traveller. Accordingly a

Fig. 16.—A somewhat oblique section of a filaria in the stomach of a mosquito; the darker object is the filaria, it has just escaped from its sheath, the more lightly shaded object lying above the free filaria.

physiological change comes over the unsheathed parasite; the wriggling movement, which had previously characterised it, is changed into a locomotive movement. This locomotive movement has for its first object to transfer the filaria to the walls of the insect's stomach. And now we understand

Fig. 17.—Two filariae lying between the muscular fibres in the thorax of the mosquito.

the object of the armature that Nature has provided the parasite with, and why she had sheathed this armature so carefully previously, and why she has unsheathed it later. When

the filaria gets to the end of this first stage of its journey and arrives at the walls of the mosquito's stomach, it employs its now naked beak and hooks to tear through this viscus, and then, boring and squeezing along and between the fibres of the thoracic muscles, to work its way to the destination where it will subsequently undergo the metamorphosis qualifying it for further life. I have many times followed out the little drama I describe. These drawings, made from actual preparations, illustrate the main facts very well.

ANALOGIES IN LIFE-HISTORIES.

Let us now see if the analogy which we have found to subsist between the structure, habits, and requirements of the filaria and the structure, habits, and requirements of the plasmodium can be made to apply to their life-histories as well. Let us see if what we positively know about the life-history of the filaria can be used for the elucidation of what we do not so positively know about the life-history of the plasmodium.

The crescents and the potential flagellated intra-corporeal forms of the quartan and benign tertian plasmodia are sheathed like the filaria to preserve them from destruction by the phagocytes while they are in the circulation, just as the filaria is preserved from destruction by its sheath. The plasmodia cast their corpuscular sheaths just as the filaria casts its sheath on leaving the human body. The flagella are now formed, and exhibit movements which lead to locomotion, just as is the case with the filaria when it has cast its sheath. These are facts about which there cannot be the slightest doubt.

The mosquito has been proved to suck up and to be an efficient liberating agent for the filaria. Similarly, the mosquito when it sucks up malarial blood must act as a liberating agent to the plasmodium. This is only what we would expect, and, moreover, it is a fact which I can easily demonstrate. Let us think out how the plasmodium would comport itself in the mosquito's stomach, using as a guide our knowledge of what happens to the filaria in similar circumstances. Assuming that the plasmodium in any of its forms is not killed by the digestive juices of the insect, and that in the insect the development of the parasite proceeds in the usual way, then the ordinary intra-corporeal parasite will go on to sporulation. I do not say it does and I do not think it does; but, for the sake of argument, let us assume it does. The sporules in due time become ripe and fall apart. What next? What useful purpose as regards the interests of the plasmodium could these stationary sporules fulfil. They are motionless and the blood is motionless, and there is no mixing up of spores with blood corpuscles as when they circulate in the human body; consequently, the spores cannot get to fresh corpuscles even if there were any corpuscles still alive. So far are the corpuscles from being alive that they are now mere shadows of corpuscles which have parted with their hæmoglobin, as we saw when studying the case of the filaria in the mosquito's stomach. Without hæmoglobin the corpuscles are unfit to house and feed the plasmodium. The spores, if they are formed, will therefore remain where they find themselves, a ready prey to the still living phagocytes; or, dying, they are digested by the gastric juices of the insect, just as would happen and does happen under similar circumstances to such filariæ as fail to cast their sheaths and quit the stomach of the mosquito. Clearly, if no other provision is made than that afforded by the ordinary intra-corporeal sporulating form of the plasmodium, so far as the mosquito is concerned, the ingested parasite comes to an end.

But as Nature has provided for the safety and developmental interests of the filaria by endowing it with locomotive properties soon after entering the mosquito, may not Nature in the case of the plasmodium also, to meet its requirements in the mosquito, have provided a similar locomotive form in the flagellum, a flagellated spore, which can rapidly pass in virtue of its locomotive properties to a place of safety and to its appropriate nidus? If this be so, then we must conclude that when malarial blood passes into the mosquito's stomach immediately the crescents and other forms of flagella-producing body will proceed to evolve, the protecting capsule will break away, flagellation will be effected, and the flagella will swim free. Analogy indicates this conclusion; the facts I shall detail in my next lecture show that it has indicated correctly.

It is interesting to note how accurately Nature has adapted the habits of the plasmodium to the conditions in which, on this hypothesis, it finds itself at this stage of its existence. Note that there is no delay in flagellation once the parasite has got out of the human body; no waiting for several hours, as in the case of the filaria, pending the complete escape of hæmoglobin into the liquor sanguinis. Flagellation occurs before the blood has undergone any material thickening, for we have seen that it occurs within a very few minutes of the blood's escaping from the body, and therefore of being swallowed by the mosquito. Although coagulation never takes place in the stomach of the mosquito, yet thickening of the blood from transudation of hæmoglobin and from absorption of its watery part does occur, the process beginning shortly after the blood has been imbibed. But this thickening is not to any great degree until some hours have elapsed, so that the evolution of the flagellum, taking place as it does within a few minutes of entering the mosquito, anticipates this occurrence. The free flagellum, therefore, finds none of the mechanical difficulties which, were its evolution delayed, might in a viscid medium interfere with locomotion.

What, still adhering to our hypothesis, we now ask is the reason for this locomotion? Why is this plasmodium spore—for spore I have tried to show that the flagellum must be—why is it endowed with locomotive properties? I will answer this question by asking another. Why is the filaria endowed with locomotive powers? The answer you know; to enable it to get to the walls of the mosquito's stomach. I believe exactly the same answer applies to the question about the reason for the locomotive faculty of the flagellated malaria spore. It is so endowed to enable it to travel from perhaps the centre of the blood constituting the mosquito's meal to the walls of the mosquito's stomach. And what, you will ask, does the plasmodium want there? What does the filaria want at the same place? The filaria is on its way to its special nidus in the insect. And so, I say, is the plasmodium. And how does the filaria get thence to its nidus? By piercing the tissues of the mosquito. And how does the plasmodium get to its nidus? Exactly in the same way; by piercing the tissues of the mosquito.

There are one or two facts about the movements of the flagellum which very much strengthen this view of its destiny. In watching flagella, both free and attached, I have sometimes been very much struck, not merely by the fact of movement, but also by the variety in the character of the movements they indulge in. These movements may be classified into three leading types: 1. The undulating spirilla-like motion that leads to locomotion. 2. A peculiar, rapidly vibrating, tetanic-like, shivering motion which the flagellum every now and then exhibits, both when attached to the parent sphere and when free. Especially is this movement seen when the flagellum in the course of its travels impinges against a blood corpuscle or other obstacle. In such circumstances the little thread straightens itself out, becomes rigid as it were, and vibrates rapidly, just as a long slender wand does when one end of it is brought sharply down on some hard resisting substance. 3. There is a third type of movement—a coiling-up movement. This, too, may be seen while the flagellum is attached to the central sphere. It coils itself up like a watch spring that has been straightened out and then released. I have, I confess, not observed this last-mentioned movement in the free flagellum, but it is not infrequently seen before the flagellum has broken loose and has often been described.

These types of movement, depend upon it, have reference to the requirements of the organism exhibiting them. They are not mere chance phenomena, designed only to puzzle and mislead the pathologist. The swimming movement we have already interpreted as subserving the interests of the parasite by transporting it to the wall of the mosquito's stomach. The rapid, tetanic-like, vibrating movement which the flagellum exhibits when it meets with an obstacle I interpret as a movement designed to pierce—a boring movement such as the filaria must indulge in when it attacks with beak and hooks the tissues of the mosquito. It must be this movement which Laveran alludes to when he says that the flagellum seems at times to attempt to penetrate those corpuscles it happens to impinge against. The third, or coiling-up movement is, I believe, a sort of rehearsal of the final act of the

flagellum drama—a drama which is concluded when the young parasite has reached its destination in the mosquito. It coils itself up then in preparation for further changes of a more passive character.

The analogy subsisting between the filaria and the plasmodium is very close, very remarkable, and I do not think I have strained it in this attempt to apply it in helping us to a solution of the problem before us. It has led us thus far in the interpretation of the life-history of the plasmodium, and, as I hope to show from actually-observed facts, I think it has led us correctly. But at this point the analogy of the filaria ceases to be a reliable guide. For a little while in their histories the two parasites are in the same dilemma, and they get out of this dilemma in the same or in similar ways. Now, however, their requirements differ, and, accordingly, their courses diverge. The filaria has to prepare to re-enter man; the plasmodium is under no such obligation, for we have seen that it can and does thrive independently of man. In the case of the filaria transference to man is, so to speak, obligatory; in the case of the plasmodium transference to man is optional. It would appear that the point at which the hitherto parallel changes, made in preparation for these somewhat different destinies, begin to diverge is attained so soon as the two parasites have fairly established themselves in the mosquito.

ANALOGIES FROM THE LIFE-HISTORIES OF SPOROZOA.

Although from this point the filaria can no longer be relied on as a guide to the life-history of the plasmodium, we are not altogether without some assistance such as analogy might be looked to to supply. We therefore turn for help to where we are most entitled to look for it, namely, to that class of organisms to which the plasmodium belongs, to which it has the greatest natural affinities—to the sporozoa; and, more particularly, to those orders of sporozoa which, like the plasmodium, are not only parasites, but cell-parasites, especially cell-parasites of insects—the gregarines and the coccidia.

The gymnosporidia, as the order to which the plasmodium belongs has been named by Labbé, are in many respects like the gregarines, in other respects like the coccidia. The members of those three orders are all of them intra-cellular parasites during a considerable part, or for the whole of their lives; they all propagate, of course, by the production of spores, and in all of them the spores have to get transferred somehow from one host to another in a more or less passive way. The gregarines and coccidia do not propagate outside the bodies of their respective hosts; I hold, therefore, as probable that their close allies the gymnosporidia, such as the plasmodium of man and the halteridium and proteosoma of birds, do not live at any time as free organisms, unless perhaps it be sometimes as a resting spore, but are always during their active propagating life parasitic. And so I consider that the reason why the plasmodium on entering the mosquito pushes for the walls of the insect's stomach is, that it may get at some cell in the mosquito's body therein to curl itself up, and grow, and sporulate just in the same way that it does in the blood corpuscles of man, and as is the habit of its allies the gregarines and coccidia. Where in the mosquito's body, and what the particular cell is, I do not pretend to be able to indicate.

Perhaps, owing to the minuteness of the objects we are dealing with, and the many practical difficulties attending the investigation, it may be long before that cell is found, and the full history of the parasite in the mosquito be thoroughly worked out; but I feel certain that these things will be established in time, and on the lines I indicate, and that the life-history of the plasmodium will be revealed as completely for the mosquito as it already has been for man.

THE ADVENTURES OF A FLAGELLUM.

So far as I know, no one has seen the plasmodial flagellum enter a cell; but that it has the desire to do so, and the power to do so, seems to be certain. I have lately received a letter bearing on this point from Surgeon-Major Ronald Ross, I.M.S., whose remarkable work on the plasmodium in the mosquito I shall fully describe in my concluding lecture. In the letter I refer to there occurs a passage which describes very graphically what I may call the adventures of a flagellum.

Referring to the examination of a certain malarial patient's blood, he writes:—

I said I was going to watch free flagella. I found one in my first specimen, and watched it continuously for three hours. So much for the statement that free flagella soon become quiescent and vanish in the serum. At first it wriggled about for twenty minutes like a trypanosoma, so that I could hardly follow it. Then it brought up against a phagocyte, and remained there so long that I thought the phagocyte had seized it. Not so; it was neither killed nor sucked in, but was actively engaged in attacking the phagocyte. The flagellum kept at this for about a quarter of an hour, and then wriggled away across two fields, and in the direction of another phagocyte. Into this second phagocyte it pushed in several places with one of its ends, and the phagocyte seemed to rear up and try in vain to get round and envelop the flagellum. At last the phagocyte seemed to give the struggle up, and flattened itself against an air bubble, the flagellum still attacking it. After fifty minutes, and when the flagellum seemed to be getting exhausted, a very curious thing happened. A third phagocyte approached, coming rapidly across the field; but it had no sooner got near than the flagellum left its fallen foe and attacked the new one, holding on to it and shaking like a snake on a dog. In one minute the third phagocyte turned sharp round and quickly made off; it went right across a whole field, the flagellum holding on. This continued for five minutes, after which the flagellum left the phagocyte. By this time the flagellum had become much more visible, and had a large swelling in the middle. I watched it steadily as its movements became gradually slower. It was certainly able to attach itself to the cover-glass (as shown by touching this with a pen) by either end, and even perhaps by the swelling. At last this swelling moved to one end nearly, and became very large and distinct until, after three hours, the creature evidently died; at any rate, it curled up and ceased to move.

Ross goes on to say:

Is not this interesting? I think it shows, first, that the phagocytes have no more power over free flagella than they have over trypanosomes; secondly, that the beast was evidently attacking the phagocytes, probably mistaking them for some other kind of cell; so I judge by its leaving the phagocytes after a time.

I agree with Ross in considering these observations most interesting; more than that, in addition to being interesting, they are highly important, for they not only establish the fact that the plasmodial flagellum attacks—that is, seeks to enter cells—but also that in the free state it can resist the phagocytes; and, contrary to the statements of many of the writers on the malarial parasite, that it does not die within a few minutes of its quitting the sphere from which it was originally emitted. It is also a curious fact that, although able to defend themselves when free, while attached to the sphere the flagella are impotent to resist the phagocytes. One often sees a phagocyte with a flagellated sphere in its interior, one or more of the flagella projecting; though for a time the flagella project, and may wave about even, yet they are securely held, and ultimately are entirely incorporated by the phagocyte. The degenerationists will have some difficulty in getting over these facts about the free flagella. Were the flagellum but a piece of degenerated protoplasm, as they maintain it is, would it live thus long, move thus actively, move with a manifest purpose? Would it resist the attacks of the phagocytes much less overthrow them?

THE PLASMODIUM A PARASITE OF THE MOSQUITO.

I think I have advanced many cogent reasons for conjecturing that the plasmodium malarie on leaving man, and as a normal step in its life-history, becomes parasitic in the mosquito, and that in this insect—as any gregarine or coccidium would do—it enters some cell, and probably develops into its reproductive sporulating form therein, just as it does in the blood corpuscles of man. What then? How can its spores get out of the mosquito so as to increase and multiply and preserve its species from extinction when, in the course of Nature, the mosquito dies? How, too, does it spread over the land, and how does it get back to man again?

Before attempting to answer these questions, I must first describe very briefly a chapter in the life of the mosquito. The female mosquito, after she has filled herself with blood—the male insect is not a blood sucker—seeks out some dark and sheltered spot near stagnant water. At the end of about six days she quits her shelter, and, alighting on the surface of the water, deposits her eggs thereon. She then dies, and, as a rule, falls into the water alongside her eggs. The eggs float about for a time, and then, in due course, each gives birth to a tiny swimming larva. These larvæ, in virtue of a voracious appetite, grow apace, casting their skins several times to admit of growth. Later they pass into the nymph stage, during which, after a time, they float on the surface of the water. Finally, the shell of the nymph cracks along its dorsal surface, and a young mosquito emerges. Standing, as on a raft, on the

empty pelt, the young mosquito floats on the surface of the water while its wings are drying and acquiring rigidity. When this is complete it flies away.

The young mosquito larvæ, to satisfy their prodigious appetites, devour everything eatable they come across; and one of the first things they eat, if they get the chance, is the dead body of their parent, now soft and sodden from decomposition and long immersion. They even devour their own cast-off skins. In examining mosquito larvæ one often comes across specimens whose alimentary canals are stuffed with the scales, fragments of limbs, and other remains of the parental insect and larval pelts.

THE HISTORY OF A MOSQUITO GREGARINE.

I am indebted to Surgeon-Major Ross for many valuable facts in support of my views as to the life-history of the plasmodium; amongst other facts, for the instructive story of a gregarine which inhabits the stomach and appendages of the Secunderabad mosquitos and their larvæ. He tracked the germs of this gregarine into the stomach of the mosquito larva, where, after an intracellular stage of short duration and which was not quite satisfactorily made out, it became a large, free, actively moving gregarine. At maturity the adult gregarines crawled out of the stomach and into the Malpighian tubes, along which they crept towards the cæcal end. There, with or without conjugation, they encapsulated themselves and generated in the interior of their capsules multitudes of pseudo-navicellæ. At maturity, which was attained at the nympha stage of the insect, or a little later in the perfect insect, the capsule ruptured liberating the pseudo-navicellæ in such numbers that they sometimes seemed completely to fill, and even to distend, the lumen of the Malpighian tubes. Many of the pseudo-navicellæ escaped in the fæces of the nymphæ; others were carried away by the mosquito when it emerged, and were emitted in the fæces of the insect, sometimes even on to the human skin while she was in the act of sucking blood. As mentioned, the development of the gregarine was sometimes effected so rapidly that numerous pseudo-navicellæ were emitted before the nymphæ stage of the mosquito was concluded, so that it was a common thing to find the empty nymphæ pelts thickly sprinkled over with multitudes of tiny gregarine germs. As we have seen that the mosquito larva devours its own and its neighbour's exuvæ, we can readily understand how, once gregarines have been introduced into a pool of water, the larval mosquitos in that particular pool become infected by the parasite. But as the mature mosquito when she quits her nymphæ husk also contains numerous gregarines, we can also understand how she, too, carries the infection with her, scattering it about the country in her fæces or conveying it to any other pool she may elect to lay her eggs and afterwards to die in. Her body is then devoured by her progeny or by any other mosquito larvæ that already chance to be in the pool. Along with the parental body the larvæ will swallow any gregarine germs it may contain, and very probably, when feeding on the mud at the bottom of the pool, may pick up other free pseudo-navicellæ.

Does not this little story of the gregarine indicate the way, or a way, in which that other mosquito sporozoon—the plasmodium malarie—multiplies? Does it not indicate how this parasite, in which man is so much interested, passes from mosquito to larva, from larva to mosquito in never-ending series? Does it not indicate how the plasmodium disease of mosquitos spreads from pool to pool and is scattered broadcast about the country; and does it not indicate how it may get back to man again?

DIFFUSION OF THE PLASMODIUM BY THE MOSQUITO.

We can readily understand how the mosquito-bred plasmodium may be swallowed by man in water, as so many disease germs are, and we can readily understand how it may be inhaled in dust. Mosquito-haunted pools dry up. The plasmodia in the larvæ, and those that have been scattered about in the water, finding themselves stranded by the drought and so placed in a condition unfavourable for development, pass into a resting stage, just as they do when by quinine or other means man is rendered temporarily unsuited for their active life. They may, probably do, become encysted as so many of the protozoa do in similar circumstances. The dried

sediment of the pool, blown about by winds and currents of air, is inhaled by man, and so the plasmodium may find its way to the human host, from whom its ancestors, perhaps, had started generations back. I would conjecture that on entering man and on entering the larval mosquito it develops into a flagellated spore similar to the flagellated spore it develops into in the mosquito's stomach. In this way it would be enabled to penetrate the mucous surfaces and get to the human blood cell.

Many mosquitos die without getting to water: all male mosquitos die without seeking water. They may die far from water, blown away, as we know mosquitos are, by high winds. The bodies of such mosquitos fall in time on the soil and decompose. The parasites they contained pass into the resting stage; and in this form they may be carried into the air by currents, or be blown about as dust, or be shaken out by man when he disturbs the soil. In this way, too, the plasmodium may find a route to man. In this way, too, we may explain the occurrence of those cases of malaria which apparently, though not really, are unconnected with swamp or stagnant water.

Such is my view of the life-history of the malaria parasite and the rôle of the mosquito with regard to it, and of the process by which man becomes infected. In my concluding lecture I shall bring forward further evidence in support of this theory, and endeavour to answer certain objections which have been, or which may be, brought against it.

PRACTICAL AIDS IN THE DIAGNOSIS OF PERICARDIAL EFFUSION, IN CONNECTION WITH THE QUESTION AS TO SURGICAL TREATMENT.¹

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SOME years ago, when honoured by a junior colleague with a request to examine one of his patients as to the existence of a pericardial effusion or of a cardiac dilatation, I happened to diagnose the case correctly; but on how insecure a ground my opinion was based I have since then realised. I can also bring to mind a painful instance—probably not unparalleled in the experience of others—in which I failed to perceive during the patient's life, though not from neglect of examination, the presence of a large effusion which should have been aspirated. This early mistake led me to work out gradually a more complete method of physical examination, which I trust others may find of as much advantage as it has been to myself.

The elements of the method are (1) accurate percussion and palpation, (2) careful auscultation, and (3) observation of the pulse. All the signs to be enumerated should be understood to apply to effusions sufficiently large to raise the question as to surgical interference. We cannot attempt today the more delicate diagnosis of slight and early effusion. Lastly, as our time is short, and our object a practical one, I must reserve all theoretical considerations, and put before you the facts with as little comment as possible.

I. PERCUSSION² AND PALPATION.

Pericardial distension taking place usually in all directions, vertically as well as transversely, the first requisite is a competent knowledge of the normal levels and lateral extensions of the præcordial dulness, a subject to which I have formerly given some attention.³

(a) *The Normal Boundaries of the Total Cardiac Dulness, and its Angles.*—The lower level of the healthy dulness is that of the junction of the xiphoid cartilage with the sternum: in other words the level of the infrasternal notch. It is identical with the "hepatic line" of dulness, or upper line of the absolute dulness of the liver (above which partial or modified hepatic dulness ranges as far as the "suprahepatic"

¹ Read before the North London District of the Metropolitan Branch of the British Medical Association.

² In working out these facts I have found Sansom's pleximeter of invaluable service.

³ Cf. *Lancet*, 1891, vol. ii, p. 473.