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ON

THE DEVELOPMENT

OF

FILARIA SANGUINIS HOMINIS,

AND ON

THE MOSQUITO CONSIDERED AS A NURSE.

BY

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On the Development of *Filaria sanguinis hominis*, and on the Mosquito considered as a Nurse*. By Patrick Manson, M.D. (Communicated by Dr. Cobbold, F.R.S., F.L.S.)

Development cannot progress far in the Host containing the Parent Worm.—Fortunately it is an almost universal law, in the history of the more dangerous kinds of Entozoa, that the egg or embryo must escape from the host inhabited by the parent worm before much progress can be made in development. Were it possible for animals so prolific as *Filaria immitis* of the dog, or *Filaria sanguinis* of man, to be born and matured and to reproduce their kind again in an individual host, the latter would certainly be overwhelmed by the first swarm of embryos escaping into the blood, as soon as they had made any progress in growth. If, for example, the brood of embryo *Filariæ*, at any one time free in the blood of a dog moderately well charged with them, were to begin growing before they had each attained a hundredth part of the size of themature *Filaria*, their aggregate volume would occupy a bulk many times greater than the dog itself. I have calculated that in the blood of certain dogs and men there exists at any given moment more than two millions of embryos. Now the individuals of such a swarm could never attain any thing approaching the size of the mature worm without certainly involving the death of the host. The death of the host would imply the death of the parasite before a second generation of *Filariæ* could be born, and this, of course, entails the extermination of the species; for in such an arrangement reproduction would be equivalent to the death of both parent and offspring, an anomaly impossible in nature.

The Embryo must escape from the original Host.—It follows therefore that the embryo, in order to continue its development and keep its species from extermination, must escape from the first host in some way. After accomplishing this it either lives an independent existence for a time, during which it is provided with organs for growth not possessed by it hitherto; or it is swallowed by another animal which treats it as a nursling for such time as is necessary to fit it with an alimentary system. The former arrangement obtains in the *Filariæ* inhabiting the

* [Throughout this memoir Dr. Manson employs the term "nurse" in the same sense as that in which helminthologists use the term "intermediate host." —T. S. Cobbold.]

intestinal canal, the *Lumbricus* and thread-worm; the latter is followed by the several species of tapeworm, and also by other kinds of Entozoa.

I find that in cases where embryo *Filariæ* are not in great abundance in the blood, we may infer that there are only one or two parent worms; they often disappear completely for a time, to reappear after the lapse of a few days or weeks. From this circumstance I infer—1st, that reproduction is of an intermitting and not of a continuous character; and, 2ndly, that the embryos, after a certain time, are either disintegrated in the blood or are voided in the excretions. The latter does occur, I know from personal investigation, in the urine; and we have Dr. Lewis's testimony that he has found the animals in the tears. In this way they may have an opportunity of continuing development either free (as in the case of the *Lumbricus*) in the media into which the excretions are voided, or in the body of another animal which has intentionally or accidentally fed on these (as in the case of the tapeworms). Man, in his turn, may then swallow this hypothetic animal or other thing containing the embryo suitably perfected, and so complete the circle. This is the history of many Entozoa; but I have evidence to adduce that, if it be one way in which *F. sanguinis hominis* is nursed, it is not the only way, and therefore probably not the way at all.

The Mosquito found to be the Nurse.—It occurred to me that, as the first step in the history of the hæmatozoon was in the blood, the next might happen in an animal who fed on that fluid. To test this idea I procured mosquitos that had fed on the patient Hinlo's blood (Case No. 46, published in 'Med. Times & Gaz.' for March), and, examining the expressed contents of their abdomens from day to day with the microscope, I found that my idea was correct, and that the hæmatozoon which entered the mosquito as a simple structureless animal, left it, after passing through a series of highly interesting metamorphoses, much increased in size, possessing an alimentary canal, and being otherwise suited for an independent existence.

History of the Mosquito after feeding on Human blood.—I may mention that my observations have been made exclusively on the females of one species of mosquito. I have never, in many hundreds of specimens, met with a male insect charged with blood. This is explained by the arrangement of the appendages and proboscis of the male mosquito, which prevents it from penetrating

the skin. As the male is provided with a complete alimentary apparatus, it is presumed that he feeds on the juices and exudations of plants and fruits. There are two species of mosquito found during the summer here: one quite a large insect about half an inch long, with a black thorax and black-and-white banded abdomen; the other about half that size and of a dingy brown colour. The former is rare comparatively; the latter is very common, and is the insect my remarks apply to. After a mosquito has filled itself with blood (which it can do, if not disturbed, in about two minutes), it is evidently much embarrassed by the weight of its distended abdomen, so that it no longer can wheel about in the air. It accordingly attaches itself to some surface, if possible near stagnant water, where it remains in a comparatively torpid condition, digesting the blood, excreting yellow gamboge-looking fæces, and maturing its ova. In the course of from three to five days these processes are completed, and the insect now betakes itself to the water, where the eggs are deposited, and on the surface of which they float in a dark-brown mass, looking like a flake of soot. The eggs do not take long to hatch (they are beautifully shaped objects, like an Etruscan vase); and the embryo emerges by forcing open a sort of lid placed at the broad end of the shell. The larvæ now escape into the water, where they swim about and feed, and become the "jumpers" we are familiar with, found in every stagnant pool.

If the contents of the abdomen are examined before the mosquito has fed, or after the food has been absorbed, the following parts can easily be distinguished:—two ovisacs containing from sixty to a hundred ova, two large glandular masses (intestine and œsophagus), and a very delicate transparent fibrous bag, the stomach. If the blood contained in the dilated stomach is examined soon after ingestion, the blood-corpuscles are seen quite distinct in outline, and behaving very much as when drawn in the ordinary way; but changes rapidly occur. First, the corpuscles lose their distinctness in outline, then crystals of hæmatin appear; corpuscles and crystals give place to large oil-globules, and the mass is deprived of its fluidity, and before the eggs are deposited all colouring-matter disappears; the white material is absorbed or expelled, and by the time the eggs are deposited the stomach is quite empty but for the embryo *Filariæ* it may contain.

How to procure Mosquitos containing embryo Filariæ.—It may be useful to those who wish to repeat and test my observations

to know the plan I found most successful in procuring *Filaria*-bearing mosquitos, and how their bodies were afterwards treated for microscopic observation. Such details may appear frivolous and unimportant; but by following them the observer will be spared disappointment, and economize his time and patience.

I persuaded a Chinaman, in whose blood I had already ascertained that *Filariæ* abounded, to sleep in what is known as a mosquito-house, in a room where mosquitos were plentiful. After he had gone to bed a light was placed beside him, and the door of the mosquito-house kept open for half an hour. In this way many mosquitos entered the "house;" the light was then put out, and the door closed. Next morning the walls of the "house" were covered with an abundant supply of insects with abdomens thoroughly distended. They were then caught below a wineglass, paralyzed by means of a whiff of tobacco-smoke, and transferred to small phials, into some of which a little water had been poured. A cover providing for ventilation was then placed over the mouth of the phial. The effect of the tobacco-smoke, if it has not been applied too long, is very evanescent, and seems to have no prejudicial influence on the posture of the mosquito. From the phials they may be removed from time to time, as required, by again paralyzing with tobacco and seizing them by the thorax with a fine pincers. The abdomen is then torn off, placed on a glass slide, and a small cylinder, such as a thin penholder, rolled over it from the anus towards the severed thoracic attachment. In this way the contents are safely and efficiently expressed, and observation is not interfered with by the almost opaque integument. If the contents are white and dry a little water should be added and mixed carefully with the mass, so as to allow of the easy separation of the two large ovisacs. These can be removed in this way by the needle, and transferred to another slide for separate examination. A thin covering-glass should be placed over the residue, which will be found to contain the *Filariæ* either within the walls of the stomach, or, if these have been ruptured by too rough manipulation, floating in the surrounding water.

Large proportion of Filariæ *ingested by the Mosquito.*—The blood in the stomach of a mosquito that has fed on a *Filaria*-infested man usually contains a much larger proportion of *Filariæ* than does an equal quantity of blood obtained from the same man in the usual way by pricking the finger. Thus six small slides,

equivalent to about one drop of bloed from the man on whom most of my observations were made, would contain from ten to thirty Hæmatozoa; whereas the blood drawn by a single mosquito, about as much as would fill one slide only, contained from twenty to thirty as a rule, and sometimes many more. One slide, in which I had the curiosity to count them, had upwards of a hundred and twenty specimens. From this it would appear that the mosquito has the faculty of selecting the embryo *Filariæ*; and in this strange circumstance we have an additional reason for concluding that this insect is the natural nurse of the parasite.

All Embryos do not attain maturity.—By far the greater number die and are disintegrated, or are expelled in the fæces undeveloped. At the end of the third, fourth, or fifth day, when the stomach is quite empty as far as food is concerned, and an embryo could not easily be overlooked, only from two to six are found in the same or slightly different stages of the metamorphosis, which I will now attempt to describe.

The Metamorphosis of the Embryo.—The embryo for a short time after entering the stomach of the mosquito retains all the appearances and habits which characterized it when in the human body; that is, it is a long snake-like animal, having a perfectly transparent structureless body enclosed in a delicate and, for the most part, closely applied tube, within which it shortens and extends itself, giving rise, from the collapse of the tube when the body is retracted at either end, to the appearance of a lash at the head and tail. In a very few hours changes commence. The tube first separates from the body by an appreciable interval, giving the appearance of a distinct double outline, and the body itself becomes covered with a delicate but distinct and closely set transverse striation. Oral movements are now very evident, not that they did not exist before, but because the slight increase of shading from the striation renders them more apparent. The indication of a viscus seen in some specimens vanishes at this stage. Presently the tube or sheath is either digested by the gastric juices of the mosquito, or it is cast off as a snake does its skin, and the animal swims about naked, and without any trace of a head- or tail-lash. The striation becomes very marked; but gradually as the blood thickens, and the movements of the embryo become in consequence less vigorous, these markings completely disappear, giving place to a peculiar spotted appearance. Each spot is dark or luminous, according to the focusing of the

microscope, and probably depends on some oily material now collecting in the body of the animal.

This concludes the first stage of the metamorphosis, and has taken about thirty-six hours to complete. During all this time the original proportions of the animal have been preserved and vigorous movement maintained. Now, however, it enters on a sort of chrysalis condition, during which nearly all movement is suspended, and the outline and dimensions very much altered. Hitherto the body was long and of graceful contour, but now it becomes shorter and broader, the extreme tail alone not participating in the change. The large spots in the body disappear, gradually giving place to what seems to be a fluid holding numerous minute particles in suspension. I have once or twice detected to-and-fro movements in these. The tail continues to be flexed and extended vigorously, but only at long intervals, whilst all oral movements cease. By the end of the third day the animal has become much shorter and broader, the small terminal portion of the tail still retaining its original dimensions, and appearing to spring abruptly from the end of the sausage-shaped body. Large cells occupy the previously homogeneous-looking body, and sometimes something like a double outline can be traced. Indications of a mouth present themselves; and if a little pressure is applied to the covering-glass, granular matter and cell-like bodies escape from an orifice placed a little in advance of the tail. The animal now begins to increase in length, and in some specimens to diminish in breadth, the growth seeming to be principally in the oral end of the body. The structure of the mouth is sometimes very evident; it is four-lipped, the lips being either open or pursed up. From the mouth a delicate line can be distinctly traced, passing through the whole length of the body to the opening already referred to as existing near the caudal extremity. Feeble movement may still sometimes be detected in the caudal appendix; but when the now growing body has attained a certain length the tail gradually disappears.

After this point, specimens of the *Filaria* in its third and last stage are difficult to procure. Most mosquitos die about the fourth or fifth day after feeding; and if their bodies, which fall into the water, are examined, they are soft and sodden and without *Filariæ*, these having either decomposed or escaped. Sometimes, however, ovulation does not proceed rapidly, and the mosquito survives to the fifth or sixth day; or perhaps death may not occur, as it usually does, soon after the eggs have been laid,

and the insect may survive this operation for two or three days. In such the last stage of the metamorphosis can be studied: four to six days seem necessary for its completion. Out of hundreds of mosquitos watched, I have been successful in finding *Filariæ* in this last stage in four instances only. In one of these there was quite a number of embryos in regular gradation, from the passive chrysalis up to the mature and very active embryo, so that there can be no doubt of the relationship of the latter to the former, though their appearances differ so much. Owing to the small number of specimens I have examined, I am not quite certain about the details of this stage of the metamorphosis. As far as I can make out, the body gradually elongates from the hundredth to the fortieth or thirtieth of an inch, and when mature it measures fully a fifteenth of an inch in length by the five hundredth of an inch in breadth.

When at the above stage large cells occupy the interior; but as development advances these become reduced in size, and accumulate round the dark line I have already mentioned as running from the mouth to the caudal extremity. In this way an alimentary tube is fashioned, and the peculiar and characteristic valve-like terminatiom of the œsophagus in the intestine, seen in the *Filariæ*, is developed. The mouth may now be seen open and funnel-shaped, and the tail is reduced to a mere stump. Movements, first of a swaying-to-and-fro character, but afterwards brisker, now begin. The body gradually elongates and becomes perhaps slightly thinner; all cellular appearance vanishes, and, owing to the increasing transparency of the tissues, the details can no longer be made out. A vessel of some sort is seen in the centre running nearly the whole length of the body, and opening close to one extremity; this extremity is slightly tapered, and is crowned with three, or perhaps four, papillæ; but whether this is the head or tail, and whether the vessel opening near it is the alimentary canal or vagina, I cannot say; the other extremity is also slightly tapered, but has no papillæ. There can be no doubt which is mouth and which tail, but the intermediate steps I have failed to trace satisfactorily. There is a stage between these two in which the mouth is closed, and the œsophagus can be seen running from it. If the body is compressed, that tube can be forced through the skin and distinctly seen; but about that time the tissues become so transparent that their exact relations cannot be made out.

I cannot say if the three or four papillæ round one extremity

of the developed embryo constitute the perfected boring-apparatus of the worm, or if it is the boring-apparatus at all; but comparing this with what is found in other species of the same genus, I think it very probable that it either is or will become the piercing-apparatus. Some time ago I operated on an Australian horse for this worm, and had the satisfaction of finding the parasite not very much injured after removal: it was an unimpregnated female possessing all the typical structures of the *Filariæ*. Its head was armed with a five- or six-toothed saw, the teeth arranged, like those in some kinds of old-fashioned trephines, in a circle round the mouth. I removed a worm from the same eye of the same horse about three or four weeks previously; the cornea had healed, and the cloudiness cleared up before the second worm appeared. I infer from this, from the very perfect boring-apparatus, and from the female being unimpregnated, that the eye is not the resting- or breeding-place of the *Filaria* found in it, but that it is sometimes accidentally entered by the worm on its travels in search of the suitable spot. From the fact that one worm succeeded the other I infer that the sexes are brought together in this way (as in the case of *Filaria sanguinolenta* of the dog): when a wandering worm comes across the tract of another, it follows it up; thus several may be found together at the end of the burrow.

Probably, then, these papillæ are the boring-apparatus to be used in penetrating the tissues of man and escaping from the mosquito. At this (presumably the final stage of the *Filaria's* existence in the mosquito) it becomes endowed with marvellous power and activity. It rushes about the field, forcing obstacles aside, moving indifferently at either end, and appears quite at home, and in no way inconvenienced by the water in which it has just been immersed. This formidable-looking animal is undoubtedly the *Filaria sanguinis hominis* equipped for independent life and ready to quit its nurse the mosquito.

Future history of the Filaria.—There can be little doubt as to the subsequent history of the *Filaria*, or that, escaping into the water in which the mosquito died, it is through the medium of this fluid brought in contact with the tissues of man, and that, either piercing the integuments, or, what is more probable, being swallowed, it works its way through the alimentary canal to its final resting place. Arrived there, its development is perfected, fecundation is effected, and finally the embryo *Filariæ* we meet with in the blood are discharged in successive swarms and in countless numbers. In this way the genetic cycle is completed.

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