SCHISTOSOMA CATTOI, A NEW BLOOD FLUKE OF MAN.*

[WITH SPECIAL PLATE.]

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WHILE I was Resident Medical Officer at St. John's Island Quarantine Station, Singapore, cholera broke out on a passenger ship from China. Some four hundred coolies were quarantined. Amongst them was a Chinaman from the Province of Fukien who presumably had never been away from China before.

He died of cholera after three days' illness. He was plump for a coolie. During life it was found that the right lobe of his liver extended two fingerbreadths below the costal margin. The left lobe was a handbreadth below the sternum, and its percussion dullness merged into the splenic. The spleen was palpable 1 in. from the iliac crest, and its notch was in line with the anterior axillary fold.

A necropsy was made an hour and a half after death. The adipose tissue throughout the body was a prominent feature. The appearance of the peritoneum suggested repeated attacks of peritonitis. The appendices epiploicae were thickened, and in some places matted together. The recto-vesical pouch was almost obliterated. Encasing the large intestine was a coat of fat, most marked at the mesenteric attachment. The mesenteric tissues were all thickened and loaded with fat. The mesenteric and prevertebral glands varied in size from a bean to a golf ball, the largest forming a cluster near the duodenum. The liver was uniformly enlarged. Its surfaces were markedly nodular, its borders sharp and irregular, the whole presenting the appearance of a very coarse cirrhosis. Its consistence was greatly increased, but its colour was not appreciably altered. The coats of the gall bladder were thickened, and a layer of fat almost completely encased this viscus, which was distended with clear mucoid, apple-jelly-like material containing several minute black gall stones. The colon was much thickened throughout. The mucous membrane was swollen, hyperaemic, and friable, presenting numerous small circular, superficial erosions and patches of necrosis. The outer coats were very tough, almost cartilaginous, and showed no tendency to ulcerate. The rectum was three-quarters of an inch thick all round, and was adherent to the bladder. It nearly filled the true pelvis. Where adhesions had formed the bladder wall was thickened, but elsewhere it was healthy, and nowhere was the vesical mucosa diseased. The sigmoid was uniformly thickened; in tracing the bowel upwards the thickening became less marked and more patchy. The coats of the caecum and appendix vermiformis were uniformly hypertrophied, the mucous membrane presenting small patches of ulceration and necrosis. The appendix was provided with a mesentery, and a distended lymphatic could be recognized running along its free surface. The liver and bowel cut gritty on section. The lower end of the ileum was thickened in patches, and

the mucosa congested over corresponding areas. The enlarged spleen was pigmented. The stomach, pancreas, suprarenals, kidneys, heart, and lungs, showed no signs of coarse disease.

As the lesions above mentioned were peculiar, some of the viscera were preserved. Sections of the liver, mesenteric lymphatic glands, and bowel (Fig. 1) were made in Singapore by Dr. Finlayson, and at the Kuala Lumpur Research Institute by Dr. Daniels. Numerous small oval bodies having a smooth, stout capsule were found. Opinions differed as to whether these were coccidia or the ova of some unknown parasite, but the case was published in the Journal of the Malaya Branch of the British Medical Association as a case of coccidiosis in man. Subsequent examination in this country of sections of intestine showed ova and filaria-form embryos in bundles in the mucosa and villi of the large intestine. These, along with other specimens, were shown at the Medical Research Club, London, but no definite conclusion regarding the nature of the oval bodies was come to. An eminent German authority, to whom pieces of tissue were kindly sent by Dr. Bulloch, stated "that the oval bodies were

neither coccidia nor the eggs of a trematode, but those of a nematode of unrecognizable species, etc." At Sir Patrick Manson's suggestion, to whom the specimens were shown, I devoted my whole time to working out the case at the London School of Tropical Medicine, where systematic examination and sections of all the preserved tissues were made. Soon after I commenced investigating, nematode embryos were found in smear preparations from the large intestine, and one was found in the vessel of a mesenteric lymphatic gland. These facts, coupled with the juxtaposition of ova—some empty—and embryos in the mucosa and villi of the large intestine, led to the suggestion of a nematode infection, but as no evidence of a differentiated embryo could be seen in any of the eggs, even in those lying in close proximity to the bundles of free embryos, one hesitated to adopt this conclusion. Subsequently, in sections of the mesocolon, I found adult trematodes, male and female, in the blood vessels (Fig. 9), the

Fig. 9.—Transverse section of a mesenteric vessel showing: M, two male schistosomes; F, females; I, caeca in male; L, caeca in female; O, ovum. Magnification 56x.

ova (Fig. 9, O) in the uterus of the female corresponding in every particular with the oval bodies found in the various viscera. It was now clear that I had to deal with concomitant trematode and nematode infections; that the oval bodies were the ova of the trematode; and that their close association with filarial embryos was merely accidental.

A preliminary paper was read and drawings with specimens exhibited at the meeting of the British Medical Association at Oxford. Later, on continuing my dissections, entire mature worms were found in the smaller mesenteric blood vessels (Figs. 4 and 5.) It was difficult to determine the nature of the vessels in which the mature parasites lay. They were manifestly blood vessels, but whether arteries or veins was not so evident. I submitted my preparations to several eminent physiologists and pathologists. Unfortunately, there was no unanimity among them as to the arterial or venous nature of the vessels. I am constrained therefore to admit that this important point is for the present unsettled. My own conviction, however, is that the parasites occur in both arteries and veins. (See Fig. 2.)

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PARENTAL FORMS.

The male (Figs. 4 and 5) is 9 mm. long, less than half a millimetre broad, and, in my spirit preparations, of a light brown-yellow colour. The measurements are only relative as they are taken from spirit specimens. Three entire adult males, with fragments of others, were found. They closely resemble those of *Schistosoma haematobium*, having their lateral borders incurved ventrally, thereby forming a canal groove along the entire length—the gynaeophoric canal—in which the female lies. The anterior extremity is blunt, with a terminal sucker in which the mouth lies. The dorsal lip of the sucker is longer than the ventral. Behind the sucker the body is slightly constricted, forming a neck. The worm attains its maximum breadth at the posterior sucker, which lies ventrally in the gynaeophoric canal about half a millimetre behind the anterior sucker, whence the body tapers gradually to a truncated posterior extremity. The posterior sucker is oval and trumpet-shaped, its long diameter being transverse; it is larger and more muscular than the anterior. Both suckers are retractile.

The alimentary system consists of a mouth furnished with a sphincter, a strong muscular oesophagus, and two caeca joining posteriorly to form a terminal ampulla. The oesophagus, surrounded by small glands, is constricted at its middle, and divides, just anterior to the acetabulum on which rests the posterior sucker, into the two caeca which run along either side of the body. Three anastomoses of the caeca were made out.

The excretory system ends in an excretory pore which is subterminal and ventral. The nervous system has not been satisfactorily determined. The reproductive system consists of a lobular testicle or testicles, vesiculi seminales, vas deferens, and genital pore with its sphincter, opening centrally into the gynaeophoric canal behind the posterior sucker.

A distinctive feature of this schistosome is the absence of ciliated warts on the integument, the presence of which constitutes so marked a feature of the African worm. Minor anatomical differences are: (a) Smaller size of the worm; (b) its longer vas deferens; (c) the characters of the testes.

The female (Fig. 4, b) is almost cylindrical (diameter 0.113 mm.), longer, more slender, and darker than the male. The cervical constriction is quite as marked as in the male. The suckers, alimentary and excretory systems, correspond with those of the male, except that the excretory pore is terminal. Owing to excessive fragility of the spirit specimen it was found impracticable to mount an entire specimen of the female worm.

The reproductive system consists of a muscular, central, elongated uterus occupying the anterior half of the body, and opening near the posterior sucker. The ova are arranged irregularly in single or in double rows. At the posterior extremity of the uterus are the shell glands and opening of the oviduct with the vitello-duct. Behind this the body bulges slightly to taper subsequently to a sharply-pointed extremity. The bulging marks the position of the ovary; posteriorly are the vitellogene glands.

From the female *Schistosoma haematobium* the following differences have been made out:

(a) The posterior sucker is larger than the anterior; the converse holds good in the *Schistosoma haematobium*.

(b) The bulging in region of ovary is more marked.

(c) The arrangement of the yolk glands is different.

In both sexes minute, highly refractile spines are seen in the suckers and at their anterior extremities.

The eggs (Fig. 7) are yellow-brown in colour, oval, measuring on an average 70 μ long by 40 μ broad. They vary between 60 μ and 90 μ in length and 30 μ to 50 μ in breadth. They have a stout, smooth shell on section. There is no trace of a spine or operculum. In the sections some of the ova were empty; others contained a central, circular mass which stained deeply; some contained cells staining at their periphery, whilst others had cells staining in the centre. These may or may not completely fill the ovum. In some cases the cellular contents were seen escaping from a ruptured ovum. In no one of the ova could distinct embryos be detected, although appearances suggestive of a developing embryo could be observed. The ova differ from those of *Schistosoma haematobium* in their colour, shape, size, and in the absence of a spine. The bilharzia ovum is of a brown colour, contains a well-developed embryo, and is larger, 0.19 mm. (Looss). Moreover, its ends are more pointed, and it is provided with a spine.

The ulcerative lesions of the bowel produced by the new species differ from the corresponding lesions of the bladder produced by *S. haematobium* in the entire absence from the

former of the fungating masses so characteristic of the latter. Further, the new species does not give rise to the perihepatic nodules as described by Sandwith in bilharziosis.

In addition to the character of the ova and to the anatomical differences already noted, there are certain other points which serve to differentiate the species.

1. The habitat of *S. haematobium* is reputed to be venous only, whereas the habitat of the new schistosome is mainly arterial; too much stress must not be laid on this point, seeing it has not been proved that the former cannot affect arteries or the latter veins.

2. The ova of *S. haematobium* affect mainly the urinary system, and escape from their human host by this channel. In the new species the ova apparently exclusively affect the alimentary system, escaping by this route from their human host.

3. In this case there is a much more general infection of abdominal viscera, for ova of *S. haematobium* have not been found in the pancreas and appendix.

4. The geographical distribution differs, for no case of bilharziosis has yet been met with in China.

Histopathology.

The parent worms are found in small groups at the bifurcations of the smaller mesenteric vessels, and partially or completely plug the vessels. In one arteriole 0.621 mm. in diameter two complete sections of the male and female are seen in *copulâ* (Fig. 9). Blood cells are occasionally seen between the wall of the vessel and the parasites.

Where ova accumulate they provoke at certain places a small-celled infiltration, which gives place later to a great proliferation of fibrous tissue. Pigment is seen in the liver and bowel. In the intestine from caecum to anus the ova occupy roughly two concentric layers—the one subperitoneal, where the ova are comparatively scarce; the other in the submucous coat, where they are innumerable, in some cases densely packed (Fig. 6). Between these zones in the muscular layers ova with their long axes at right angles to the bowel lie in single or in double rows. Ova are plentiful in the mucosa, are more numerous in the necrotic areas, and are seen apparently in process of extrusion (Fig. 8) at the margin of an ulcer.

Of the intestinal tract, the rectum and appendix are most affected; the distended lymphatic vessel in the appendix already referred to is choked with ova. Everywhere throughout the small intestine ova were found, but only in patches and in relatively small numbers.

The obliteration of the rectovesical pouch was probably caused by the irritation produced by ova accumulating in vast numbers in the wall of the rectum. In the many sections examined no ova were found in the vesical mucosa, though they were present in small numbers in the outer coats of the bladder.

In the liver the ova are plentiful, lying singly or in larger or smaller clumps embedded in the markedly hypertrophied fibrous connective tissue.

In many of the enlarged mesenteric lymphatic glands ova were found in the thickened trabeculae.

In addition to the localities already mentioned ova were found in the outer wall of the gall bladder, in the pancreas, liver capsule, fibrous coat of the larger mesenteric vessels, mesentery, pylorus, duodenum, jejunum, and ileum. Several sections were made of the round ligament of the liver and of the diaphragm without any ova being found.

Doubtless the life-history of the new schistosome corresponds with that of other trematodes, the geographical range of the intermediary host being the principal determining factor in its distribution.

That this case is unique is extremely improbable. When proper search has been made doubtless many additional cases will be found in the natives of the endemic districts. As a ready means of ascertaining the degree of prevalence and geographical range of the infection I would suggest systematic examination at *post-mortem* examinations of scrapings from the mucous membrane of the bowel, preferably of erosions or ulcerated patches. With a low power of the microscope only a few minutes are required to determine the presence or absence of the ova in such preparations.

The ova have probably been found many times in the course of ordinary microscopical examinations of faeces, but have been mistaken for the ova of *Ankylostoma duodenale*, which they closely resemble.

It is interesting to note the accumulation of filariaform embryos in the villi, probably in the lacteals, of the intestinal tract, and their presence in faeces. I am not aware of any similar observation.

Diagnosis.

Sub Kingdom...	...	Vermes.
Class ...	...	Plathelminthes
Order ...	...	Trematoda.
Family ...	...	Schistosomidae.
Genus ...	...	Schistosoma.
Species ...	...	Schistosoma Cattoi (Blanchard) 1904.

Measurements given below are from specimens found in hardened tissues:

	Female.	Male.
Length ...	?	9 mm.
Breadth ...	0.115 mm.	0.447 mm.
Breadth (near ovary) ...	0.134 mm.	—
Diameter at neck ...	0.041 mm.	0.180 mm.
Gynaecophoric canal ...	absent	entire length of body
Shape and size of posterior sucker	0.061 by 0.047 mm.	0.290 by 0.189 mm.
(long. diam. longitudinal)	(long. diam. transverse)	
Shape and size of anterior sucker	0.51 mm. circular	0.124 mm. circular
Distance between centres of these	0.146 mm.	0.552 mm.
Genital pore...	behind posterior sucker	behind posterior sucker
Excretory pore ...	terminal	subterminal
Tubercles and cilia ...	absent	absent
Spines in suckers...	present but scarce	present

Habitat of Adults: Mesenteric vessels.

Ova: Oval with rounded ends and smooth stout capsule, destitute of spine and operculum.

Size: 0.065 to 0.090 mm. by 0.030 to 0.050 mm.

Found in intestinal tract and its appendages.

Number of Cases: One.

Symptoms: Probably colic and dysentery.

Physical Signs: Enlarged liver and spleen.

Geographical Distribution: Province of Fukien, China.

Type Specimen: Museum of London Tropical School of Medicine. Mounted in xylol balsam unstained from preserved formalin tissue.

It is possible that the filariaform embryos above referred to also escaped into the lumen of the bowels from the ulcers, for on making smear preparations from various parts of the bowel these embryos were found. In one smear thirteen embryos were present but in many others none were found. These embryos had the following measurements and characters; these, however, cannot be taken as accurate as none were got in fresh state.

Average length ...	0.300 mm.
Greatest thickness ...	0.008 "
Sheath ...	present.
Shape of head ...	truncate conical.
" tail ...	sharp pointed.

(The sheath in many cases could not be seen, but embryos may discard it when in unnatural surroundings.)

Ova of trichocephalus dispar, ankylostoma duodenale, ascariis lumbricoides, in numbers, were found in the smears. Adult worms of all these were also found in the bowel.

I am deeply indebted to Sir Patrick Manson for much encouragement and criticism; and also for his sending specimens to the International Zoological Congress at Berne, where they were examined by Professor Blanchard, Drs. Loos, Ward, Stiles, Grossi, Monticelli, and other zoologists, who all agreed that the parasite was a schistosoma and new to science. Professor Blanchard has done me the honour of naming this new helminth *Schistosoma Cattoi*. To Drs. T. S. Kerr and E. E. Henderson the credit is due for the excellent drawings and photomicrographs.

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AN INVESTIGATION

INTO THE

NATURE OF THE FOLLICLE CELLS OF THE MAMMALIAN OVARY,

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[PRELIMINARY NOTE.]

THE primary object of this paper, which the writer regards as one of a preliminary nature, is to state as briefly as possible the results of an investigation into the nature of the follicle cells of the mammalian ovary. This investigation was from

the first and has thus far been carried out on hypothetical grounds, as one of a series of other investigations connected with certain of the many problems which a student of cancer is called upon to face.

The term "follicle cells" is here intended to imply only those cells that go to form the zona glomerulosa and the discus proligerus of the Graafian follicle. The term is not intended to include the ovum itself, or those cells of the interstitium that enter into the formation of the investing layer.

The ovaries examined have been chiefly those of the rabbit, but sufficient attention has been paid to the ovaries of the bitch, cat, sheep, and sow, to show that the follicle cells in all these animals are of the same essential nature, and it is therefore reasonable to regard what is to be described as typical of mammals in general.

After a careful investigation extending continuously over the last three months, and involving the examination of many hundreds of nuclei belonging to the follicle cells of the mammalian ovary, the writer has been led to believe that the type of mitotic division prevailing in these cells is heterotype—that is to say, that these cells partake of the nature of germ cells as regards, at any rate, their method of dividing, and that the mitotic figures are characterized by exhibiting the halved or reduced number of chromosomes. These chromosomes are of a coarse nature as compared with those of the body generally (somatic cells), and resemble closely those that occur in the heterotype cell of a cancer or sarcoma, as recently described by Farmer, Moore, and Walker; while the general character and the method of division is similar to what obtains in the parent cells of the ovum or spermatozoon.

The ovaries employed were transferred immediately after killing the animal to the fixing reagent. Various fixing agents were employed, the best results being obtained with Hermann's platino-osmic acetic mixture. In one case the fixing was carried out *intra vitam*, according to Mann's direction, with a mixture of picric acid, corrosive sublimate, formol, and water. The stain employed was chiefly iron-haematoxylin, the process being that recommended by Heidenhain. Owing to the smallness of the follicle cells and to the minute size of the chromosomes, decolorization was in some cases carried almost to vanishing point, the division of the mitotic figures being previously marked. By this means a more accurate opinion could be formed as to their delineation, shape, and disposition.

The coarse nature of the chromosomes has already been referred to. As seen *en masse* in metaphase, anaphase, or telophase, this character becomes the more obvious when compared with similar phases as revealed by a somatic cell. The polar views of the follicle cells show the distribution of the individual chromosomes more clearly, and their reduced number becomes the more apparent. By counting the chromosomes in serial sections this number, in the case of the rabbit, would appear to be about eight or rather more—that is to say, eight chromosomes are distributed to each pole respectively. The exact number, however, was very difficult to determine, but the evidence was sufficient to show that the number corresponds to the reduced, halved, or heterotype number, and not to the full somatic number, as seen in somatic cells or in cells of the body generally. The individual chromosomes are comparatively large as compared with the somatic type, their apices are rounded, not sharp and pointed. When arranged at the equator in metaphase they appear as small spherical bodies, sometimes in more fortunate specimens they suggest ring-shaped bodies. In anaphase the chromosomes present the appearance of horseshoes, though they are often irregular, one limb being longer than the other.

It has thus far been impossible to determine accurately the earlier and later phases in these follicle cells, no definite proof of a dividing nucleus exhibiting the somatic number of chromosomes could be established either in metaphase or anaphase, and it would almost seem as if the cell division is carried on throughout with a reduced number of chromosomes. Occasionally, however, a figure resembling the later stage of somatic prophase may be seen. On the other hand, the majority of the prophases, like the other phases, are suggestive of the heterotype process, and many cells present an appearance that would suggest "tetrad" formation as seen in an oocyte or spermatocyte.

As further evidence of the germ-cell nature of this tissue it may be noticed in certain very young follicles—those that consist of a single layer of follicle cells surrounding an ovum and which are apparently at a stage immediately preliminary to assuming active growth—that two

Fig. 1.—Ova in intestinal submucosa. At first taken to be coccidia.

Fig. 2.—Section of mesentery. Worms seen lying in blood vessels in transverse and longitudinal section. Note difference in thickness of vessel walls.

Fig. 3.—Magnified view of Fig. 2, showing transverse section of blood vessel with worms *in situ*. Note smooth cuticle.

Fig. 4.—Male worm with a portion of female.
A. Male worm showing caeca.
B. Female.

Fig 5.—Male worm. Note smooth cuticle.

Fig. 6.—Section of appendix (stained), showing ova in masses, a dense submucous layer, and a less-marked subperitoneal layer.

Fig. 7.—Magnified view of Fig. 5, showing ova.

Fig. 8—Ova in process of extrusion from intestinal mucosa.