

THE OCCURRENCE OF SCHISTOSOMA JAPONICUM VEL CATTOI IN THE PHILIPPINE ISLANDS.

By PAUL G. WOOLLEY.

(From the Serum Laboratory, Bureau of Science.)

As long ago as 1887 Maxima, in Japan, wrote of a peculiar form of liver cirrhosis which was caused by an unknown parasite. In succeeding years his observations received corroboration from various sources. The ova of this parasite were found not only in the liver but also in other organs, and it soon became apparent that the observers were dealing with a definite endemic disease which was more or less closely confined to the Provinces of Bingo, Yamanaishi, Hiroshima, and Saga. From a town in Bingo (Katayama) the malady has taken its name, so that in Japan it is known as the "Katayama disease."

In 1904 Katsurada studied fifteen cases of the infection, and in the stools of five found ova which resembled those of *Schistosomum hamatobium*. Later, in dissecting dogs and cats from an infected district, he encountered (in a cat) flukes within the portal vessels. These he described (August 30, 1904) in a Japanese paper, in which he proposed the name *Schistosomum japonicum* for the parasite. Later, in December, 1904, Katsurada published again on this subject, this time in German, and stated that Fujinami had announced (October, 1904) the discovery of a female *S. japonicum* in a human subject. In the same year, in lesions of the liver, mesenteric glands, and intestines of a Chinaman from the Province of Fukien, China, Catto, at that time resident medical officer of the Singapore quarantine station, found certain bodies which he believed to be coccidia. The case was first reported as one of coccidiosis, but later this diagnosis was changed, and in September, 1904, the claim was set forth that the bodies were the ova of a new parasite. Later still, Blanchard, after seeing Catto's specimens, gave the trematode the name of *Schistosoma cattoi*, and in 1905 Catto described it under that title. Catto based his description upon material obtained from the human subject, while Katsurada based his largely upon that obtained from cats, and this distinction, as Stiles insists, must be taken into consideration.

This being the case, the conclusion is fairly safe that the parasites described from Japan and China are of the same species. It also seems

assured that they are quite different from the Egyptian form *S. hamatobium*.

Here it is only necessary to say that the worms are characterized by the absence of the ciliated warts on the integument, which are a marked feature of *S. hamatobium*. Minor anatomic differences are the size of the worm [average 10.43 millimeters (Katsurada)], the length of the vas deferens, and the lobular character of the testes.

The eggs are smaller than those of *S. hamatobium*, have blunter ends, and no spine.

A complete comparison of the Chinese and Japanese worms and of their ova will be found in Stiles's paper.

The description of the clinical symptoms of the disease "Katayama" must, for the present, be taken from the Japanese reports, since in neither Catto's nor my case was there any opportunity for clinical study.

Katsurada was able to examine from 30 to 54 cases every year while stationed in the infected district, in which his residence extended over about five years. He observed but few deaths (three to five annually) which he considered were directly due to the parasite, but he regards the indirect mortality as much higher. Defective physical development is the rule in affected children. Diarrhœa is usually the first symptom to be noted, while anemia and ascites generally follow later; however, the most striking feature is the shape assumed by the trunk. The hypogastric region seems to shrink, while the epigastric enlarges, a transverse furrow forming directly above the umbilicus, so that the general appearance of the abdominal region is that of an inverted gourd. Dilatation of the epigastric region and of the lower part of the thorax was noted even in patients whose liver and spleen were not much enlarged. The commonest symptoms are an initial increase in the size of the liver, followed by a decrease, a secondary enlargement of the spleen, a muco-sanguinous diarrhœa, severe attacks of ascites, and progressive anemia. Katsurada found the ova of the parasite under discussion and also those of *Tricocephalus dispar*, *Uncinaria*, and *Ascaris lumbricoides* in the stools of his patients.

Yamagiwa described (1890) a case of Jacksonian epilepsy in which he found ova in certain nodules in the brain. These ova were similar to those now known to occur in "Katayama." At the time Yamagiwa first reported his case he considered these ova to be those of the lung distome, but he now believes himself to have been dealing with *Schistosoma japonicum*.

In Catto's case the right lobe of the liver extended for a distance of two fingers' width below the costal margin and the left lobe a hand's breadth below the sternum. The spleen was enlarged.

My case occurred in a native Filipino who had not been out of the Islands and who at the time of his death was in Bilibid Prison. He died suddenly of a terminal bacterial infection in the course of intestinal amoebiasis and uncinariasis. The liver was not enlarged, but the spleen was somewhat increased in size.

The pathologic details of the Japanese cases, as described by Katsurada (Scheube), are as follows:

At autopsy the liver is less than normal in size and its surface is marked by small nodules, larger than those observed in Laennec's cirrhosis and smaller than those of the usual gross form. The capsule of Glisson is thickened. Microscopical observation shows connective tissue increase and round-cell infiltration in the capsule of Glisson in which the ova lie, in part in the lumen or in the walls of the portal capillaries and in part in the connective tissue. There are also fibrous nodules and tubercle-like areas which contain ova, although these are not commonly seen in the parenchyma. In addition to their location in the liver, the eggs are also found in the intestinal wall (especially that of the large intestine), in the mesentery, in the mesenteric glands, the lungs, and the brain. In the intestinal wall they especially occur in the submucosa and often are present in such numbers as to cause the mucosa over them to become bulged out or even eroded. Kanamori (Scheube) found in one case, in the rectum and sigmoid, adenomas resembling the new growths described by Kartulis in *Bilharziosis*. In the lungs and brain the eggs are encountered in tubercle-like masses, surrounded by round-cell infiltration and an increase of connective tissue.

In Catto's case the liver and spleen were both enlarged. The condition of the peritoneum suggested that repeated attacks of peritonitis had occurred. The appendices epiploicae were thickened and in places were matted together. The recto-vesical pouch was almost obliterated. The mesenteric lymph glands were enlarged. The liver was apparently cirrhotic. The colon was thickened and its mucous membrane was swollen, hyperæmic, and friable, and presented small circular, superficial erosions and patches of necrosis. The rectum was adherent to the bladder. The mucosa of the ileum was congested and formed thickened patches. The stomach, pancreas, adrenals, kidneys, heart, and lungs showed no gross lesions. In sections of the liver, mesenteric glands, and bowel small oval bodies were found which were at first believed to be coccidia. Subsequent examination disproved this and showed them to be the ova of a trematode. Nematode embryos were found in smears from the large intestine and in the vessels of a mesenteric lymphatic gland. In sections of the meso-colon, adult trematodes were found in blood vessels, and in the uterus of one of these were oval bodies corresponding to those seen free in the tissues in other sections. The parent worms were encountered in small groups at the bifurcations of the small mesenteric vessels. Where the ova had accumulated in certain places they had provoked a small-cell infiltration which gave rise to a proliferation of fibrous tissue. In the intestine, from caecum to anus, the ova roughly occupied two concentric layers—the one subperitoneal where they were comparatively scarce, the other submucous where they were innumerable. They were also plentiful in the mucosa, and more numerous in the necrotic areas, in which situation they were seen apparently to be in the process of extrusion.

The rectum and appendix were the parts most affected in the entire intestinal tract. Ova were found throughout the small intestine, but only in patches and in comparatively small numbers. They were plentiful in the liver, lying singly or in large or small clumps embedded in the hypertrophied fibrous tissue. They were also found in the thickened trabeculae of many of the enlarged mesenteric glands. Ova were also encountered in the outer wall of the gall bladder, in the pancreas, liver capsule, the fibrous coat of the mesenteric vessels, mesenteric, pylorus, duodenum, jejunum, and ileum. Ova of *Trichocephalus dispar* and *Ascaris lumbricoides* were also seen in the bowel.

The case to be described was one of the series which formed the basis of a report on the pathology of intestinal amœbiasis by Dr. Musgrave

and the writer. During the investigation of the pathologic anatomy of that disease I discovered the presence of the ova which, in the opinion of Shiga, Fujinami, and Stiles, are those of *S. japonicum* v. *cattoi*.

The autopsy was performed by Dr. Musgrave a few minutes after the death of the patient. There was an old, discharging abscess on the right arm and another on the right side of the thorax extending into the pectoral muscles. The subcutaneous fat was well preserved and the muscles were somewhat pale. The left lung showed an intense congestion, with oedema of the lower lobe. The right was also congested and an abscess, over which the two layers of the pleura were firmly adherent, was present in the lower lobe, binding the lung to the diaphragm, ribs, and sternum. The cavity of this abscess, resembling those seen in amebiasis, was filled with a thick pus. The abdominal cavity was free from adhesions. The walls of the intestine were somewhat thickened and the mesenteric lymphatics moderately enlarged. The spleen was enlarged and a well-marked chronic perisplenitis was present; it was adherent to the diaphragm, and its surface was wrinkled and pale. The liver showed a considerable perihepatitis and was bound to the diaphragm and abdominal wall by firm adhesions. On the dome was a large scar resembling that resulting from a healed abscess; about this were old and dense adhesions. On section, the liver was pale and cloudy, giving an increased resistance when cut. The kidneys showed a moderate parenchymatous degeneration. The stomach and the small intestine showed a well-marked catarrhal condition, and in the former there were a few small hæmorrhages. In the upper 40 centimeters of the small intestine there were a number of uncinaria. The large bowel gave evidence of amebic infection throughout, but the most marked pathologic changes were in the transverse and descending colon, and less in the cæcum and rectum. In the most advanced lesions the process simulated a hæmorrhagic enteritis in which small superficial ulcerations predominated. These ulcerations displayed a considerable variety, but the deep-sloughing, undermined ulcer was not present. The appendix was not involved. (Musgrave.)

Microscopically, large numbers of amæbæ were found in scrapings from the ulcers and in the intestinal contents, but none could be demonstrated in the pulmonary abscess. Ova of uncinaria were also present in the intestinal contents.

Tissues from the intestine, liver, and lungs were secured and preserved in Kaiserling's solution. Bits of these were embedded in celloidin and paraffin. Sections were stained with hematoxylin and eosin.

The histological study showed that the mucous membrane of the large intestine was atrophied and, in areas, eroded. The submucosa was thickened and oedematous. The muscular layers presented but little change. The ova occurred chiefly in fibroid tissue in the submucosa, where they were innumerable and surrounded by round-celled infiltration. In the

mucosa they were much fewer, in the subperitoneal layer very infrequent, in the muscular layer absent. In the liver they were confined almost entirely to the perivascular tissues, and were most commonly seen about the intralobular vessels. They also occurred about the interlobular vessels and in the parenchyma. In the lungs they were found only in the tissue about the abscess cavity and were seen in but very small numbers. Wherever they were present they were surrounded by small-cell infiltration and fibrosis.

The following comparative measurements of the ova were furnished to me by Dr. Shiga, after he had examined my specimens and compared them with those of Fujinami and Manson:

	Manson.	Fujinami.	Woolley.
Length.....	<i>mm.</i> 0.0728	<i>mm.</i> 0.0662	<i>mm.</i> 0.0624
Breadth.....	.048	.0436	.0436

In the opinion of Katsurada these parasites feed upon the blood and in this way produce the anæmia which, according to the Japanese reports, is a common symptom of the disease. He also (see Stiles) suggests that the worms probably form a toxin which perhaps is the cause of the enlargement of the liver. The eggs may form embolisms in various organs, most frequently in the liver, in which they cause inflammation and increase in the connective tissues, producing a type of cirrhosis in which the surface of the organ is coarsely and irregularly granulated. These changes assist in bringing about more or less prominent portal stasis. The eggs in the mucosa and submucosa of the intestine, especially of the colon, cause more or less severe inflammation; resulting in part in the destruction, in part in the formation, of tissue, changes which are sometimes followed by the tumor-like growths described by Kanamori, and sometimes by ulcers.

Katsurada believes that the disease originates from stagnant water. He says that in summer the water standing in the rice fields becomes covered with bubbles which break when in contact with the skin, with resulting itching and eruptions. Infection, then, he thinks takes place through the abraded skin. In places where artesian-well water is used and where the people do not wade in the bubble-covered water the disease is becoming less frequent.

Since visiting the farming districts of Japan I have little doubt but that the disease is a water-borne one and that it originates in the rice fields or irrigated gardens. The same is true of China. In both these countries the fields are fertilized by human excreta to such an extent that in many places traveling is most unpleasant because of the odor. Under such circumstances the opportunities are excellent for the transmission of a disease which is caused by a parasite the ova of which are

passed in the stools. Whether infection occurs through the skin or not is still a question, though from the distribution of the eggs in the body we would suppose that it occurred by the gastro-intestinal route. However, the same is true of uncinariasis, and still there appears to be considerable evidence of the occurrence of the latter infection through the skin.

The significance of this new case is evident. It means that not only in China and Japan but also in the Philippines there is a disease caused by a blood parasite which may of itself, or by its eggs, and perhaps also by a toxin, produce a serious condition resulting in cirrhosis of the liver, splenomegaly, ascites, dysentery, progressive anaemia, and also, possibly, epilepsy of the Jacksonian type. In certain stages of the infection the condition may be confused with tropical splenomegaly, of which it possibly is one of the much-sought-for causes; or with amoebic dysentery or uncinariasis, with either or both of which it may be combined, or with epilepsy. It is very probable, now that a case has been encountered, that further ones will be discovered, and perhaps it will be found to be nearly as common, both in China and the Philippines, as it is in Japan.

The following method of staining the ova in the tissue was devised by Mr. Willyoung, of the Biological Laboratory:

Celloidin sections were immersed in water and then stained in a solution containing 1 per cent acid fuchsin and 2 per cent oxalic acid. They were then washed in water and stained in an aqueous solution containing 0.12 per cent of aniline blue and 1.2 per cent oxalic acid. Differentiation was accomplished by using acid alcohol and 80 per cent alcohol. By this means the ova were stained a brilliant red and the tissue a clear blue.

SUMMARY.

In lesions in the lungs, liver, and the bowel of a Filipino, ova have been found which agree in shape, size, and color with those of *Schistosoma japonicum vel cattoi*.

The lesions in the bowel were ulcerations closely resembling those seen in some forms of amoebiasis; those in the liver were characterized by fibrosis.

The symptoms were not definite, because of the mixed infection with other intestinal parasites.

From these observations it follows that in China, Japan, and in the Philippine Islands there is a trematode worm differing characteristically in its morphology from the allied African species, which produces lesions, especially in the large intestine and liver, and which has been described as *Schistosoma japonicum vel cattoi*. The case under observation is, to the best of my knowledge, the first schistosoma infection encountered in the Philippine Islands, and, therefore, now that it has been called to the attention of investigators, it seems not unlikely that other cases will be discovered.

Since the above was written, a second Chinese case of schistosomiasis has been recorded by Hayer (*Amer. Med.* (1905), X, 578). This case was first observed by O. T. Logan, of Chungteh, Hunan, China, who made clinical notes upon the case and who later sent these and specimens of the feces to the Naval Medical School. The patient, a boy of 18 years, for six years had bloody stools. At 15 years of age he had been incapacitated for hard work. Logan found the liver and spleen enlarged, the latter but slightly. The stools, which continued to show blood, averaged about four in twenty-four hours and were preceded by abdominal pain. The ova of the parasite were found in the feces, and each ovum contained a ciliated embryo. Logan thought the ova were those of *S. japonicum*, and in this view Stiles, Lovering, and Beyer coincide.

From the following articles I have drawn very generously, and to Dr. Stiles and Dr. Shiga I wish to express my gratitude:

CATTO: *Schistosoma cattoi*: A New Blood Fluke of Man. *Brit. Med. Jour.* (1905), I, 11; *Journ. Trop. Med.* (1905), VII, 70.

SCHREIBER: Ein Neues Schistosomum beim Menschen. *Arch. f. Schiffs- und Tropen-Hygiene* (1905), IX, 150.

STILES: The New Asiatic Blood Fluke (*S. japonicum*, 1904; *S. cattoi*, 1905) of Man and Cats. *Amer. Med.* (1905), IX, 821.

KATSURADA: An Endemic Disease Caused by a Special Parasite Previously Unknown in Japan. *Sci. I. Kaul.*, XXIII and XXIV. (Review in *J. A. M. A.* (1905), XLV, 80.)

LOOSS: *Schistosomum japonicum* Katsurada, Eine Neue Asiatische Bilharzin des Menschen. *Centr. f. Bakt., Orig.* (1905), XXXIX, 280.

ILLUSTRATIONS.

- FIG. 1. Ova in the periportal connective tissue of the liver. Hematoxylin. (Photomicrograph.)
2. Ova in the interlobular perivascular connective tissue of liver. Hematoxylin. (Photomicrograph.)
3. Ova in the parenchyma of the liver lobule. Shows small-celled infiltration and commencing fibrosis. Hematoxylin. (Photomicrograph.)
4. Ova in lung. Hematoxylin. (Photomicrograph.)
5. Ova in mucosa and submucosa of large intestine. Shows atrophic and infiltrated condition of mucosa. Hematoxylin. (Photomicrograph.)

In all instances the photographs were made with the Zeiss photomicrographic apparatus, compensation ocular No. 6, objective AA; bellows at 45 centimeters.



Fig. 1



Fig. 2

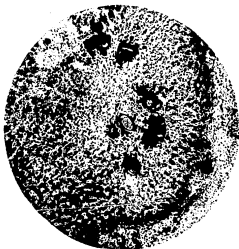


FIG. 3.

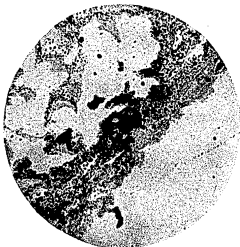


FIG. 4.

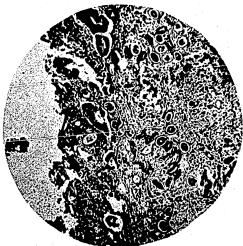


FIG. 5.