



NOTES ON THE CONDITION OF THE LIVER IN SCHISTOSOMIASIS.¹

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I. INTRODUCTION.

Schistosomum japonicum was discovered and described as recently as 1904, although the disease which it produces had been recognized in Japan for nearly two decades previously. Outside of a small area in Japan, cases of infection with this blood fluke are still so infrequently seen that each one is worthy of report and discussion, as such reports will aid in locating the geographical distribution of the parasite and in clearing up its life history and pathologic effects. In discussing the present case, we wish to speak particularly of the pathologic findings in it and in other recorded cases, and to draw a contrast between these and those of infection with the closely allied *Schistosomum hæmatobium*.

II. CASE RECORD.

The patient, P. O., was admitted on January 16, 1908, to Dr. Ruffner's service in the Division Hospital in this city, and died on the following morning. He was a Filipino soldier 30 years old, belonging to a Visayan Scout company, single, and a native of Calbayog, Samar, in which town he lived continuously until his twenty-fourth year. He then enlisted and during the six years of his service was stationed on the Islands of Panay, Cebu, Leyte and Samar. He had never been out of the Visayas except for short visits, and he was on furlough in Manila when he entered the Division Hospital. The sick record of his company shows that during the six years of his service he was in hospital one hundred and nineteen days and in quarters eighty-three days, although the causes of admission to sick report are not given.

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When he was admitted to the Division Hospital he was suffering from diarrhoea and cramps. His heart action was weak, rapid and irregular, and a diagnosis of myocarditis, probably due to beriberi, was made.

Autopsy by Dr. Whitmore three hours after death of the patient. The body is well developed and well nourished and, with the exceptions hereafter noted, the organs present no macroscopical alterations. Upon opening the abdomen, the *liver* and *spleen* are found to be moderately enlarged, the latter being somewhat adherent. The liver is not cirrhotic in appearance, but presents pale patches over its surface, and, more particularly, many whitish nodules varying in size up to the head of a pin, and situated under the capsule. On excising and crushing these nodules, oval eggs are found measuring approximately 70 by 40 μ . On section, many more nodules are seen scattered throughout the entire organ. The small intestines harbor a small number of hookworms; they present no gross changes, while the large intestine shows only one small area situated low down in the bowel, where the mucous membrane is swollen and injected. The bowel contents show ova similar to those in the liver, but these are few in number, and ova of uncinaria are also present.

Histologic examination.—Tissues were secured from the liver, kidneys, lungs and intestines. These were preserved in Kaiserling's solution and in formalin, imbedded in paraffin, sectioned and stained with hæmatoxylin and eosin and with Bismarek brown and eosin. A microscopic study of the liver shows the presence of ova either in groups or singly, usually occurring in the interlobular connective tissue (Pl. I, fig. 1), but also occasionally throughout the parenchyma, and in one instance an ovum is found apparently lodged in the intralobular vein. There is a considerable increase in the connective tissue around the lobules and encroaching upon them. The staining of the tissue is irregular, being quite faint in places.

The most striking feature is the presence of the miliary nodules noted above. (Pl. I, fig. 2.) These tubercular-like nodules are mentioned by Katsurada, but are said to occur rarely in the parenchyma. Our sections show them situated exclusively in the parenchyma occupying the place of a lobule or of two or more lobules fused together. The central area stains deepest, and is composed of an indefinite mass of nuclei, red blood cells and fibrin. It is quite sharply defined from the next zone which is made up of young connective tissue radiating toward the center. This zone gradually merges with a ring of still younger connective tissue belonging to the interlobular tissues. Some nodules have a small center and are evidently being gradually walled off and replaced by new connective tissue growth beginning at their peripheries. Throughout this connective tissue there is a new formation of bile channels, apparently an effort to repair the damage to the lobule. Ova are usually present in small numbers in these nodules. (Pl. I, fig. 3.)

Sections of the large intestine show the presence of ova in small numbers in the submucosa, accompanied by a moderate increase in the connective tissue. They occur in small groups outside the vessels close to the *muscularis mucosa*. Ova are also found in the mucosa lying close to the epithelial cells of the glands of Lieberkühn. The muscular layers are apparently unchanged. No ova are found in the small intestine nor in the other tissues. The ova in the walls of the intestine seem much more compressed and distorted than those in the liver. The vessels of the mesentery of the large intestine were carefully searched for the adult parasites, but without success.

Measurements were made of a number of the ova in the tissues, and they were found to average 62 μ in length by 39 μ in width, dimensions which are approximately those give by Stiles, Woolley, Katsurada and

Catto in their accounts of the ova of *Schistosomum japonicum*. They were studied in comparison with a section of the liver from Catto's case, which shows ova of a similar appearance.

III. PATHOGENESIS OF THE CIRRHOSIS OF THE LIVER.

It is clearly evident that in this case the liver was the organ to bear the brunt of the infection, the invasion of the intestinal walls being of but secondary importance to the lesions in the liver. In this respect the findings here are in accord with those hitherto reported in cases of this malady. In the earliest Japanese writings on the disease, the latter is described as a peculiar cirrhosis of the liver due to a parasite, while Katsurada, in his original description, speaks of it as an affection of the liver both of man and of cats. In the case described by Catto, the extreme enlargement of the liver and spleen was noted during life, while at autopsy, although there were marked changes in the other organs, especially in the large intestine, the cirrhotic condition of the liver was perhaps the most striking feature. In Woolley's case, the first to be described in the Philippine Islands, the liver was smaller than normal and markedly cirrhotic. In both of these instances numerous ova were found in the perivascular tissues of the liver, where they apparently caused a marked hypertrophy of the connective tissue. In two of three cases reported by Dr. Logan in China, enlargement of the liver was a prominent feature of the malady while in all three, œdema of the legs and ascites were present, possibly due to hepatic diseases. This list includes all the reported cases that have come to our knowledge, and in practically all of them changes in the liver have been found either clinically or by post-mortem examination.

The pathogenesis of the cirrhosis in these cases is difficult to establish. A moderate increase in the interlobular tissues might be due to the presence alone of the ova, but how can we account for the destruction of whole lobules in the presence of but a very few ova? The anastomosis of the blood vessels within the lobule is so free that it is difficult to see how the ova, acting as emboli, could produce this result, but Katsurada, according to Stiles, believes this to be the explanation of the cirrhosis, although he speaks also of a toxin which he thinks is elaborated by the worm and which plays a part in producing the liver changes.

IV. COMPARISON OF INFECTION WITH SCHISTOSOMUM JAPONICUM AND SCHISTOSOMUM HÆMATOBIUM.

Let us contrast the pathology of the above case with that encountered in Bilharzia infections. Madden, in his excellent monograph on Bilharzia, devotes a score of pages to the pathologic anatomy of the intestinal and urinary tracts, and in four lines disposes of the liver with the statement, "Kartulis and Symmes have described a periportal cirrhosis as having occurred in this disease." Scheube says that the ova have been

found in the liver, with slight eirrhotic changes. Manson speaks of the occasional presence of small numbers of ova in the liver, but knows of no pathological change caused by their presence. Other writers on the subject are a unit in regarding the liver as a negligible factor in Bilharziosis.

The question immediately suggests itself, why, in Bilharzia disease, should the ova cause such profound changes in the intestines and bladder, to the practical exclusion of alterations in the liver, while, in a disease as closely allied as the one under discussion in our paper, the liver should be the chief site for the lodgement of the ova and its pathology the chief features of the malady?

Dr. Letulle has published an extremely interesting article³ in which he worked out, with the most faithful attention to details, the histologic changes in a case of intestinal Bilharziosis, and from them drew some convincing conclusions. It is not our purpose to discuss the process of reasoning by which these conclusions were reached, and, therefore, we will give only his explanation of the local distribution of the ova and the resulting pathologic changes. According to his idea the pair of worms, with the female occupying the gynocophoric canal of the male, habitually inhabit the larger venous radicles of the portal system. When the time comes for the deposition of the ova, the worms, still together, migrate to the smaller veins until, having reached such a vessel of a caliber of about 1,000 μ , the male can go no further because of his size. The female then leaves the male and migrates as nearly as possible to the lumen of the intestine or bladder, that is, into the venules of the submucosa where the vessels are narrowed to 80 to 120 μ , and where she can go no farther. She takes position in one of these small veins, completely blocking it, and produces a stasis in the vessels ahead. She attaches herself by her suckers to the intima of the vessel and evacuates her ova into the distal portion of the vein. The pressure of the mass of ova, as well as that of the blood, enable their spines to pierce the walls of the vessels, and the whole mass is forced into the perivascular tissue so quickly, according to Letulle, that although he saw many masses just without the vessel, he did not find a single ovum within the lumen. The female having deposited her ova and waited a sufficient length of time for their migration, joins the male in the large vessels.

Let us apply these facts to *Schistosomum japonicum*. Here we have a similar pair of worms of the same relative size, although both are somewhat smaller than in the Bilharzia species. Although it is not proved that *Schistosomum japonicum* inhabits exclusively or even habitually the arterial side of the pelvic blood supply, Catto found worms in the arterioles in this location, and we have Manson as an authority for their

³ *Arch. de Parasit.* (1905) 9, 329.

presence on the arterial side. Now let us conjecture that the female, leaving the male in the larger arteriole, migrates into a small vessel which she will just occlude. Attaching herself as in the case of *Bilharzia*, she deposits her ova, not into a venous radicle, but into the distal side of the arteriole where the ova will be aspirated onward, the more so as in this case they are not provided with spines. Finally they reach the intervening capillaries which have a caliber of perhaps 12 to 20 μ , while the ova which must pass, measure, on the average, 40 μ . If the pressure on the mass of ova is sufficiently great to force a portion of their numbers through the vessel wall, it is not unlikely that another part will be forced through a distended capillary, especially as under the latter circumstances they would be compelled to pass through a distance of no more than 0.5 millimeter before larger venous radicles would be reached, this distance being the average length of a capillary. Having successfully passed the capillaries, nothing would intervene until the liver was reached, where all but the exceptional ovum would lodge. The fact that these exceptions exist, as is proved by the occasional ovum found in the lungs, kidneys and elsewhere, strengthens the evidence of their passing through the capillaries of the pelvis. The marked difference in the pathology of the two diseases, bilharziosis and schistosomiasis, may therefore depend first, on the location of the parasites: the one in the venous and the other in the arterial side of the portal circulation; and, second, on the morphological difference in the ova.⁴

V. GEOGRAPHICAL LOCATION.

There is nothing in the history of the case we report that is of any assistance toward clearing up the mystery of the mode of infection, nor, on the other hand, anything inconsistent with the theory put forward by the Japanese physicians that the infection is acquired by contact with stagnant water containing the embryos of the parasite. From the relatively small number of ova present it is fair to infer that the infection we studied was of a comparatively recent origin, and that it was acquired after the patient joined the military service. The Scout companies in the Visayas have performed much active duty in the field during the past few years and probably have frequently found it necessary to wade stagnant pools similar to those described by Katsurada as being the habitat of the embryo of this parasite.

⁴Professor Akira Fujinami has recently published an article on *Schistosomum japonicum* in which he states that the usual habitat of the adult parasite is in the portal system, it having been found by him in the intestinal veins, the mesenteric veins, the branches of the portal vein within the liver, and in the splenic vein. It therefore appears as if the morphology of the ova, rather than the location of the adult parasite, is the chief factor in the distribution of the ova in the tissues of the body.

The most important fact in the history is the continuous residence of the patient in the Visayas and the practical certainty of his having acquired the infection in that part of the Philippine Archipelago.

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ILLUSTRATIONS.

PLATE I.

- FIG. 1. Ova of *Schistosomum japonicum* in connective tissue of the liver. $\times 380$.
2. Miliary nodule in the liver. $\times 100$.
3. Nodule showing presence of ova. $\times 8$.



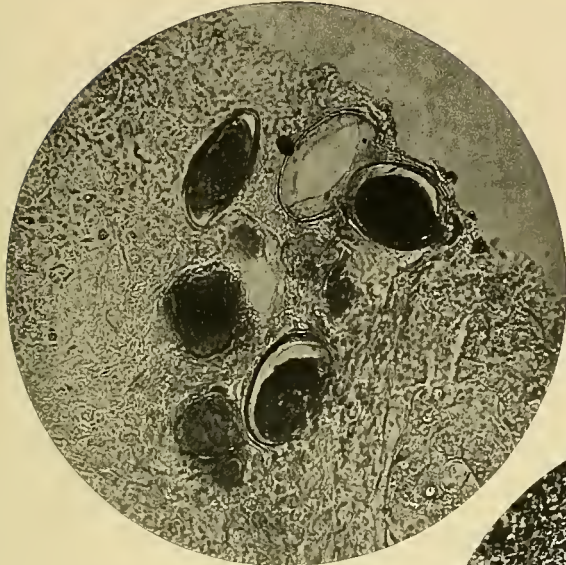


FIG. 1.

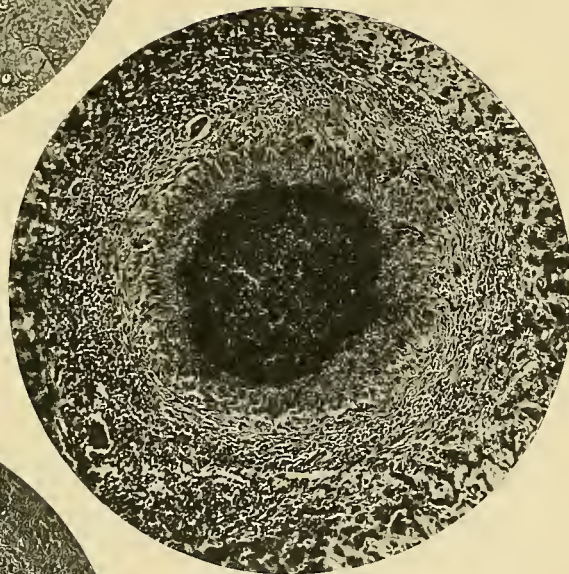


FIG. 2.

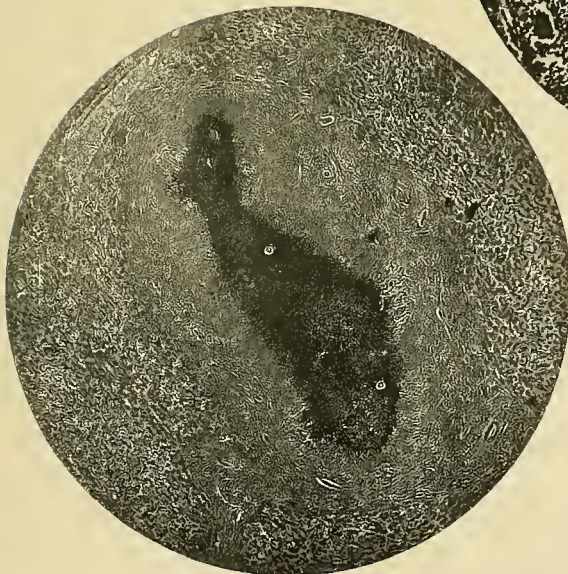


FIG. 3.

