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THE PATHOLOGY OF BILHARZIASIS *

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BILHARZIA; OBSERVATIONS ON ITS PATHOLOGY

Egyptian hematuria has been known from the very earliest times. Bilharz, working in Egypt in 1831, discovered a trematode worm in the mesenteric vessels of men who suffered from this disease and gave us the first accurate description of the parasites. In 1894, Looss[10] described the parasites more fully and outlined the life cycle in the human body. The mode of transfer from patient to patient was not fully investigated until Leiper,[9] working in the bilharzia mission in Egypt in 1915, discovered that in common with other parasitic trematodes, the bilharzia parasite is transmitted from host to host through an intermediate host. In this case the intermediate hosts are small fresh water snails of the genus bullinus and genus planorbis.

There are three closely related trematodes of the genus Schistosoma that are now known to produce characteristic lesions in man. *Schistosoma japonicum* occurs in the far East. The other two, *Schistosoma mansoni* and *Schistosoma hematobium* occur in Egypt and along the eastern coast of Africa to the Cape. The disease is found all along northern Africa and in the Congo, but most commonly in Egypt. It occurs in the West Indies and in Central America. Throughout the rest of the world occasional cases occur, but they are usually imported from some area where the disease is endemic. The disease is limited in its distribution by the distribution of the intermediate host and the habits of the people with regard to exposure to water that is contaminated.

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Conditions in the Nile valley, particularly in the delta region, are peculiarly favorable to the distribution and propagation of the bilharzia parasite. The congestion of population and primitive habits of the people insure gross contamination of the water; the tropical climate and perennial irrigation insure a wide distribution of the intermediate hosts of the parasite, and the agricultural habits of the people insure the adequate exposure of the skin to water containing infective forms of the parasite. For these reasons the incidence of infestation in a land like Egypt is very high, particularly among the peasantry.

Ferguson [7] in 1913 stated that in more than 600 postmortems on male subjects, performed in the medical school in Egypt, no less than 61 per cent of the males between 5 and 40 years of age were infested. Madden [12] in 1910 said that 10 per cent of the total mortality in Egypt was due to bilharzia. He points out the fact that his figures are based on the number of deaths occurring in the hospital, and as very many ill patients go home to die, and are therefore not included in the record, the percentage is undoubtedly much higher. Of 3485 native patients treated in the American Hospital at Tanta since 1924, 35.3 per cent were treated for bilharzia and its complications. The incidence of the disease among the peasantry of the country is much higher than these figures indicate, for there are patients with mild infection who complain of no symptoms and yet occasionally pass blood and ova in the urine and feces.

The American Mission Hospital is situated at almost the geographic center of the delta of the Nile and affords an ideal opportunity to see a large amount of bilharzial material both clinically and in the laboratory. Approximately 1200 native patients are housed for periods varying from one to three weeks during each year. A large number of these patients come suffering from advanced bilharziasis. Surgical intervention is often necessary for the relief of complications arising from the infestation. The material from which this study was made was collected over a period of five years residence in Tanta. All specimens removed surgically were examined and the more interesting of them preserved in 10 per cent formalin and brought to America for further study. They were cut, embedded in paraffin, sectioned, and stained with hematoxylin and eosin in the laboratory of the City Hospital in Cleveland.

All of the specimens were from native Egyptians and contained

bilharzia parasites. Many of them were polypi removed from the rectum and bladder. In many cases of inguinal hernia, the peritoneal sac was found to be infiltrated with ova. Where this was the case the sacs were kept for study. In the course of laparotomies for bilharzial tumors, specimens were removed from the abdomen. These specimens consisted of markedly involved epiploic appendages, pieces of omentum and peritoneum containing nodules of ova. In cases where the vermiform appendix was removed from native patients, it was always examined for bilharzial and amebic infections. Interesting specimens showing bilharzia in the female genital tract were obtained during the course of gynecological operations for other than bilharzial conditions. The effects of oviposition under the squamous epithelium of the vagina were studied in sections obtained from cases of marked vaginal polyposis by means of the curette. Sections from the margins of perineal fistulae near the anus and about the scrotum were used to study the effects of ovaposition under the true skin. Four partial autopsies on patients who died in the hospital furnished the rest of the material.

The study is based, specifically, on a series of sixty-five specimens that show the intestinal mucosa; fourteen specimens of tissue including the peritoneum; twelve vermiform appendices, and forty other tissues from various parts of the body. All of the tissues in this series showed bilharzial involvement.

In order to understand the pathology of bilharzia, it is necessary to know the life history of the parasite that causes it. In general the two species known in Egypt are very similar and one description will, for our purpose, suffice for both. A more detailed description is found in "The Practice of Medicine in the Tropics" by Byam and Archibald.

The Life History of the Parasite

The animal is a bisexual trematode. The male is a white to gray worm, 1 to 1.5 cm. long. The anterior portion of the body is cylindrical and is armed with an anterior and ventral sucker. The portion of the body posterior to the ventral sucker is leaf-like when spread out and terminates in a rounded blunt extremity. In the natural condition this flattened posterior portion of the body is rolled in from the two sides, forming a longitudinal ventral groove, the gynecaproic canal. The result is a rounded appearance. (Figs. 1 and 5.)

The female parasite is filamentous, cylindrical in shape and much longer than the male. Two suckers, similar to those described for the male, are seen toward the anterior end of the body. In nature the female is usually partially enveloped by the male and lies in the gynecaproic canal (Figs. 2, 3, 4). Both the male and the female parasite have a very primitive alimentary canal beginning at a stoma in the anterior end of the body and ending blindly posteriorly. The anatomy of the generative organs differs somewhat in the different species, but in general is similar. The ovary is located in the posterior half of the female worm and the oviduct passes forward to join the vitelline duct. The uterus extends anteriorly to the genital pore, just posterior to the ventral sucker.

The ova measure about 0.15 by 0.06 mm. and are just about the lower limits of visibility to the naked eye. Those of the species hematobium have a terminal spine (Fig. 13), and those of the genus mansoni have a lateral spine (Fig. 8).

The parasites attain their adult form in the liver and vessels of the portal system. When mature they migrate against the blood stream till they reach a capillary bed. Selection is apparent in that *S. mansoni* migrate to the capillary bed under the mucosa of the colon and rectum, and *S. hematobium* to the mucosa of the urogenital tract, particularly of the bladder.

In Tanta, Egypt, where these observations were made, double infections are common, and *S. hematobium* ova (terminal spined) are commonly found in the feces associated with the ova of *S. mansoni* (lateral spined). Dew,[3] has pointed out the ease with which females of *S. hematobium* can migrate through the veins of the pelvic plexus to the region of the lower rectum and anus, in explanation of this fact. Fairley,[4] has pointed out the frequency with which *S. hematobium* ova occur in the feces of patients who are not infected with *S. mansoni*. *S. mansoni* ova occur in the urine, but only in heavy infestations and much less commonly than in the feces. In the year 1926 a record was kept of the routine feces and urine examinations that were made in Tanta Hospital. Many of these were single examinations and therefore the results cannot be taken as indicating the total incidence of infestation. The results are interesting in that they give an index to the relative frequency with which the two types of parasite occur in the branches of the pelvic venous plexus and the inferior mesenteric veins (Table I).

In the study of tissues the selective deposition of ova is still more clearly evident. Both in cut sections and in tissues digested by 5 per cent alkali the general region from which the tissues come can be determined by the character of the ova present. In tissues from the bladder, lower third of the ureters, urethra and genitalia, practically all of the ova in the cases studied in this series were terminal

TABLE 1

Examinations Showing Distribution of Ova in Urine and Feces

Number of Feces Examinations 860		Number of Urine Examinations 888	
Positive for *S. mansoni*	Positive for *S. hematobium*	Positive for *S. mansoni*	Positive for *S. hematobium*
267 or 31%	31 or 3.6%	20 or 2.2%	302 or 22.8%

spined. In tissues from the rectum, around the anus and in the vagina, both lateral and terminal spined ova were found, the former predominating. In the mucosa of the colon, in the parietal and visceral peritoneum, retroperitoneal lymph nodes, spleen and liver, lateral spined ova greatly out-numbered the ova of *S. hematobium* and in many cases the latter were not found.

In oviposition the female parasite forces the anterior end of her body into the smaller capillaries as far as she can and then deposits her ova. The ova are left in the dilated capillary space as the female withdraws. The elastic vessel walls close down on the ovum, forcing its sharp spine against the wall. The abrasion and a peculiar irritating quality that the ovum seems to possess cause a severe inflammatory reaction, swelling of the tissue, and finally ulceration of the epithelial covering, allowing the ovum to escape into the bladder or gut as the case may be. In a land like Egypt the ovum then readily passes into the water of the canals and streams.

The ovum itself is innocent of any ability to infest a new human host either by contact or by ingestion. If allowed to dry, it quickly perishes, but in fresh water it hatches almost at once into a miracidium. This is a unicellular ciliated form in some ways resembling a paramecium. It swims around rapidly in water but quickly perishes if it does not find a suitable host. Such hosts abound in the waters of Egypt. The fresh water snails of the genus bullinus and genus

planorbis are readily attacked and infected. Four to five weeks after infestation of the snail there emerge from its body cercariae. These are small tadpole-like forms that are just about visible to the naked eye and can be seen easily with the hand lens. This form swims about in the water for from twenty-four to thirty-six hours. Before the end of this time they must find a new human host or they perish. Contact of water harboring this form of the parasite with any surface of the body or the mucous membranes of the mouth and throat leads to infestation. The cercariae attach themselves to the skin or mucous membrane by means of their suckers, lose their tails, and penetrate to the subcutaneous lymphatics. They then start on a course of migration in the body and in about six weeks the adult forms may be found in the liver and portal veins, completing the life cycle (Leiper[9]).

It is not known just how long the parasites continue to live and produce eggs in the tissues of the host. It is evidently quite a long period, perhaps years. It is certain that individuals who have long been away from sources of infestation in countries where the disease does not exist still pass living ova in the urine and feces. In one case, known to the author, a young Egyptian student who contracted the disease when a boy continued to pass living ova during the years of his study of medicine in America and was still passing them when he returned to Egypt.

Clinical Manifestations

When the initial infection occurs there is a definite irritation of the skin due to the passage of the parasites. This is perhaps more marked in Japan than Egypt. At any rate, it has been described by Japanese writers who study the skin lesions in those who work in the rice paddies. In Egypt, skin lesions are seldom noticed and the patient does not seek medical aid because of them. As a rule, too, the infestation is so gradually acquired that the skin lesions are neither very widespread nor extensive at any one time. As the parasite penetrates into the deeper tissues, a small inflammatory nodule may be felt for a short time. Leiper describes an inflammatory skin lesion occurring in experimental animals exposed to bilharzial cercariae.

If only a few parasites have found an entrance to the body in a given exposure, the invasion is not attended by subjective symptoms.

If a massive invasion occurs there will be fever and malaise (Fairley[4]). In one case in our experience where a patient had been kept away from his home environment until he was free from infestation, and then allowed to return to his village, he went to work irrigating the fields and was exposed to heavy bilharzia infestation. A few weeks later he began to suffer from a severe typhoid-like fever with jaundice and marked prostration. Enteric fevers were ruled out by serologic tests and on clinical grounds. As he gradually recovered from his febrile attack, he developed symptoms of severe generalized abdominal bilharziasis with both types of ova in the urine and feces. A similar febrile course during invasion by the parasites has been described in foreign soldiers who have bathed in the canals of Egypt (Fairley[4]), and in sailors who, while on leave, bathed in fresh water lakes in China (Laning[8]).

In most cases the infestation of the individual begins in early childhood and continues throughout life. The peasantry are constantly exposed and constantly adding to their parasitization. If the number of parasites is not excessive, the host is able to bear his infestation fairly well, but when the infestation is excessive or complications set in, he succumbs.

Pathology of Bilharzia

The early lesions of bilharzia are due to the presence of the parasites and their ova in the tissues. The later lesions are due to disturbances of structure and function arising from the efforts of the body to throw off the infection and to repair the damage. Later lesions are also the result of bacterial invasion of devitalized tissues. The first clinical evidence of oviposition is passage of blood, which is caused by an inflammatory reaction in the mucosa either about the trigone in the bladder, or in the rectum, or in both. Soon there develop small areas of a sandy nature surrounded by hyperemia, or still more frequently the whole mucosa loses its normal bright appearance and becomes sandy (Fairley[4] and Madden[11]). The sandy appearance is due to clumps of ova lying in the tunica propria beneath the mucosa. The deposit of ova may extend until the mucosa looks like very fine sandpaper. In the bladder and ureters, urine salts are sometimes deposited on such a surface, giving rise to the foundation for a stone. Mucous membranes thus filled with ova are easily abraded and bleed readily. In order for the ova to escape

from the tissues, the mucosa must be broken through. Our studies show that this is accomplished by a process of ulceration. An intense inflammatory reaction occurs with the accumulation of many leucocytes, lymphocytes and endothelial cells. Among the leucocytes is a large number of eosinophiles. Irritation of the mucosa and the loss of its normal resistance to bacterial invasion result in actual abscess formation. The abscesses are as a rule very superficial. As they rupture into the lumen of the intestine or bladder, they discharge ova together with their contents. Granulations spring up at once in the ulcerated areas and may become excessive. As they grow they continue to carry ova up through the mucosa to the surface. From the fact that adult parasites are commonly found in the loose areolar tissue under such areas of ulceration and granulation tissue, and from the large numbers of ova in such a place, it seems likely that the gravid female is attracted to areas where the processes of tissue repair are active. The presence of bilharzia parasites and their ova seems to stimulate the tissue to activity.

The softer the mucous surface and the more glandular its epithelium, the easier it is for ova to pass through it. The columnar epithelium of the colon affords the easiest access to the outer world and ova are discharged in very large numbers through lesions in its surface. There is always excessive production of mucus, and in many areas the intestinal epithelium shows mucinous degeneration (Fig. 14).

The ova are aided in passing through the bladder mucosa by the distension and contraction of the organ, and by superficial ulceration. Abscess formation, such as is seen in the rectum, has not been noted in the bladder sections studied. In the cervical and vaginal mucosa it is more difficult for ova to escape from the tunica propria into the vagina. In our specimens small abscesses were seen to have formed around groups of ova. Small fistulae allowed the contents to escape into the vagina. Polyps are formed in the mucous membranes of the colon and the bladder. Their formation depends on the degree of infestation and on peculiarities in the reactivity of the host. They vary in size, and are often so large and numerous as to cause marked obstruction of the bowel. Specimens 3 to 4 cm. in diameter were commonly seen. The polyp may consist of a single lobule or it may be multilobular. The pedicle of the polyp may be very narrow and consist mostly of mucous membrane, in which case it is very friable;

or it may be broad and involve the deeper coats of the intestinal wall, in which case the polyp is likely to be very firm and fibrous. The lobules are covered with mucous membrane except for areas of ulceration where there is an abundant formation of granulation tissue.

In the Tanta cases polyps were found anywhere in the large intestine from the cecum to the anus, but were most often found in the descending colon, sigmoid and rectum. They occurred in a localized area or sometimes there was a diffuse polyposis of the whole intestine. In the bladder, polyps occurred less frequently than in the colon. They were located on the posterior wall near the trigone and were often associated with a malignant change. Very heavy infiltrations of the mucous membranes of the bladder and intestine sometimes occurred and resulted in a general thickening of their walls without the formation of polyps. In such a case the bladder had become a thick-walled non-contractile viscus with limited capacity and very septic walls. The sepsis is accentuated by the decomposition of blood and pus in the residual urine and a fatal issue is almost a certainty.

Microscopically the rectal polyp is seen to consist of a swollen, hyperplastic epithelium covering an irregular mass of connective tissue stroma. The epithelium is often broken by areas of granulation tissue and areas of mucinous degeneration of the goblet cells in the mucosa (Fig. 14). The stroma of the polyp is filled with bilharzia ova and in the vessels at its base there often are adult parasites of both sexes. If the polyp has been recently formed and is soft, a large number of polymorphonuclear cells, eosinophiles and lymphocytes are found in its stroma, and the ova appear undegenerated and intact (Fig. 6). If the polyp is older it is firmer, with a large amount of fibrous tissue in the stroma infiltrated chiefly with endothelial cells and lymphocytes (Fig. 11), and many of the ova are degenerate, the embryo is lost, and only the chitinous wall remains. The chitinous walls of ova are often surrounded by giant cells of the foreign body type and by pseudotubercles (Figs. 7 and 9).

Ova are much less frequently deposited under squamous epithelium than under either columnar or transitional epithelium. On the cervix, in the vagina and about the anus, however, such deposits are not uncommon. The ova are found in the corium and layers of the superficial fascia and are surrounded by an inflammatory reaction

and hyperplasia of the squamous cells. The result is a marked thickening and wrinkling of the surface. The papillae are hypertrophic and extend deeply into the corium. The epithelial thickening grossly resembles widespread confluent verrucae. Sections show the microscopic structure to be not unlike that of verrucae. As the thickening progresses, the tissues lose their vitality and small abscesses form about groups of ova in the corium. This is undoubtedly brought about by invasion of pus-forming bacteria. Abscesses form and the ulceration allows the offending ova to be discharged. The invaded area becomes very thick and edematous, with small and larger abscesses forming and rupturing on the surface. There is considerable production of granulation tissue and later of scar tissue. The epithelium becomes excessively thickened and rugose. Such a process, after it has continued for a long time, obliterates the normal structures. Cases are frequently seen in Egypt where the posterior and anterior culs-de-sac of the vagina are obliterated and the cervix is buried in a mass of scar tissue. The vagina itself may become constricted, causing more or less complete atresia.

Still less frequently ova are found deposited under the true skin. This occurs in the region of sinuses and other chronic inflammatory processes near the anus and about the genital orifices. Here, as under the moist squamous surfaces, there is no escape for the ova except through ulceration. Ova are not found in the epithelium but are seen closely related to the epithelial cells in an area of granulation or degeneration.

In all heavy infestations, ova are deposited in the muscular and serous coats as well as in the submucosa. Here the ova are in an abnormal situation and cannot escape from the tissues, so their life cycle cannot be completed. They are held prisoners, so to speak, in the tissues. The result is similar to that seen when other foreign bodies are deposited in the tissues. There is first an inflammatory reaction that is not suppurative. Large numbers of polymorphonuclear cells, lymphocytes and endothelial cells appear about the ova (Figs. 6, 8). Then, as the ova die, giant cells are seen (Figs. 7, 9). At times leucocytes and giant cells may be seen surrounding or actually within the ovum. Probably the leucocytes play a part in the removal of the embryo. The more resistant walls of the ovum remain unchanged or become calcified. Endothelial cells and lymphocytes become grouped about them and finally they are walled

off by dense fibrous tissue (Figs. 10, 11). These are the pseudotubercles very commonly seen in bilharzia tissue.

Grossly the tissue becomes hard and fibrous, cuts with a gritty feel, and presents a sandy appearance.

The peritoneum may be thickly studded with tubercles, usually distributed most abundantly throughout the lower abdomen and over the colon. These hard nodules varied in size in the specimens studied from those that could be scarcely seen by the naked eye to masses of tumor-like structure the size of a fetal head. The large masses involved all the walls of the intestine and the surrounding tissues, all being matted together in an inseparable mass. Some sections of severely involved intestines looked grossly like tumors, but microscopically showed only massive infiltration with ova, pseudotubercle formation, and excessive formation of fibrous tissue. The pseudotubercles did not show caseous necrosis.

In the interlobular veins of the liver the presence of the parasites and possibly products liberated by them causes, first, a marked enlargement, and later a peculiar periportal fibrosis, described as a pipestem cirrhosis (Symmers[13]). In young children and young adults, the liver extends down to the umbilicus and fills the whole upper right quadrant of the abdomen. In later life and in older patients the liver is smaller and nodular. Grossly it is coarsely lobular and very firm. It cuts with very much increased resistance, and throughout its substance are very marked bands and cords of fibrous tissue about the portal spaces. Dew [3] describes all grades of tissue change in the liver from a mild generalized fibrosis with hepatic enlargement such as is seen in earlier and milder cases and especially in connection with *S. hematobium* infections, to the severe periportal cirrhosis seen in later severe infections with *S. mansoni*. The specimens examined in this study were of the severe type and the periportal cirrhosis was very marked. All of these cases were heavily infested with *S. mansoni* parasites and showed pronounced intestinal involvement.

Microscopically the portal spaces showed a decided proliferation and tortuosity of the bile ducts. The veins were dilated and contained parasites. There was a great increase of the fibrous tissue which contained large numbers of lateral spined ova. In one case examined, the cords of fibrous tissue surrounding the portal spaces were two to three centimeters in diameter. Contraction of these

bands had resulted in compression of the liver parenchyma and reduction in the size of the organ. The liver cells were atrophic, due to compression, and endothelial cells contained a brown pigment.

Splenic enlargement is commonly, but not constantly, associated with bilharzia infection. It is apparently most common in *S. mansoni* infections. The average weight of the spleen in five cases at Tanta where the spleen was removed surgically was 1168 gm. The organs were firm and uniform in consistence, cut with increased resistance, and presented a pulp that did not scrape away readily. Microscopically there was evident increase in the amount of fibrous tissue. The follicles and trabeculae were widely separated and the splenic pulp was very cellular and fibrous. No parasites or ova were seen. The cells were mainly of the endothelial type and contained a brown pigment that was similar in nature to that found in the enteric canal of the bilharzia parasite (Manson-Bahr[1]), and in the endothelial cells of the liver.

In severe infestations ova are found deposited in all abdominal organs. In this study they have been found in the walls of the small intestine, appendix, cecum and colon; in the pancreas, liver, retroperitoneal lymph nodes and omentum; in all points of the peritoneum, particularly over the colon, bladder, and in the sacs of inguinal herniae; in the ureters, bladder, seminal vesicles, epididymis, testes, ovary, uterus, cervix and vagina. Ova have been discovered in the lungs, brain and kidneys.

The later complications of bilharziasis are those that often cause the greatest debility and bring about a fatal issue. In itself bilharzia is not likely to be a lethal disease. The most frequent complications occur in the urinary system. One of the early manifestations of bilharzia infection is swelling about the ureteral openings into the bladder. Stasis in the ureters and kidneys follows. Bleeding into the bladder and ulceration of its mucosa sooner or later results in cystitis. Long-continued irritation of the bladder wall causes thickening and loss of elasticity. Residual urine and blood in the bladder result in still further sepsis. Ascending pyelitis and pyonephrosis are very common sequels. Deposits of urine salts occur and stones are formed in kidney, ureter and bladder.

Inflammation about the trigone and urethra causes swelling and later strictures which interfere with emptying the bladder. Abscesses form about the trigone and in the prostate. Extravasation

of urine occurs and abscesses and later sinuses form in the perineum and scrotum. Frequently cases were seen where extravasation caused the scrotum to slough away, leaving the testes exposed. In one case the extravasation extended up in the abdominal wall as high as the umbilicus, resulting in severe sepsis and death.

About the anus and rectum, abscesses and sinuses are common. Stricture of the rectum is frequent as the result of trauma to the walls of the gut. Polyps in the intestines cause the patient to go to stool constantly, and the straining results in relaxation of the perineal muscles, edema of the gut and prolapse of the intestines. As much as eight inches of the lower bowel have been seen protruding from a patient after he has been at stool. One of the specimens studied was from such a case. Constant straining during his illness had caused marked prolapse of the lower bowel. A conical mass of swollen, ulcerated, everted intestine protruded from the anus, which was much dilated. After death the bowel was removed. The lumen was found to contain bilharzial polyps. The mucosa was very much inflamed, in areas ulcerated, and contained large numbers of ova. The walls of the intestine and the surrounding fascial supports were edematous and contained bilharzia ova and an inflammatory exudate.

Ileus is common, due to adhesions about the intestine or to actual narrowing of its lumen by fibrosis or by polyps.

Abscess formation in the liver or abdomen has not been noted. Bilharzial appendices sometimes become septic and are difficult to treat surgically because of the low resistance of the surrounding tissue.

Thrombosis of the veins is common. It may occur in the mesenteric veins and cause an ileus and gangrene of the gut. Cases were seen in which the femoral vessels, abdominal vena cava and portal vessels were involved. In one specimen studied there was extensive mesenteric thrombosis and thrombosis of all branches of the portal veins in the liver. The vessels contained large numbers of parasites.

In our experience the blood in bilharziasis shows anemia that is out of proportion to the blood losses from the bladder and bowel. In cases of average severity the hemoglobin ranges between 30 per cent and 45 per cent, the red count from less than one million to three million. The white count is usually about 10,000 to 12,000 and there is a marked eosinophilia. Day,[2] in his report on the blood

changes in bilharziasis, selected early and uncomplicated cases and concluded that bilharziasis *per se* produces only slight anemia, and the most characteristic change is eosinophilia.

Tumors are commonly seen associated with bilharzial tissues. Ferguson,[6] and Madden,[11] call attention to the tumors of the bladder and say that both sarcoma and carcinoma occur. True carcinoma of the bladder has frequently been seen during this study and in at least two instances tumors that look very much like sarcomas were found in the bladder.

In the colon and rectum two examples of mucinous carcinoma were seen, one in the appendix and the other in the rectum.

Discussion

The study of this material was undertaken in the hope that the character of the pathologic processes resulting from the presence of bilharzia parasites and their ova in the tissues might be more clearly understood. The following points have been more clearly brought out.

1. It has been recognized that the presence of the parasites and their ova in the tissues is attended by a primary inflammatory reaction of a nonsuppurative nature. We wish to point out that whether this inflammation is followed by ulceration or fibrosis depends on the location of the deposition of ova. We believe that there is no inherent quality in the parasites or the ova that is sufficient, of itself, to produce ulceration. The ulcerative process seems to be dependent on the action of secondary bacterial invaders on tissues of diminished vitality. Where the tissues are not exposed to such invasion as, for example, in the peritoneum, omentum and deep tissues like muscle, abscess formation and the discharge of the ova do not commonly occur. Where they do occur, the process begins with suppuration in more superficial tissues. In superficial tissues near the epithelial lining of a hollow viscus or even under the skin, the primary inflammation is followed by ulceration and discharge of the ova.

In the deeper tissues and in the abdominal organs such as the liver, abscess formation has not been seen. The ova, at first surrounded by inflammatory cells, become isolated by fibroblasts and giant cells of the foreign body type. The ultimate result is the formation of a granuloma, the characteristic unit of which is the bil-

harzial pseudotubercle. The excessive fibrosis often resulting late in such a process produces marked distortion or even obliteration of structures, interferes with physiologic function and is the basis of many of the serious complications occurring late in the disease.

2. That the bilharzia parasite produces nocuous substances in the body of its host is evident on the basis of clinical experience with patients who have acquired a severe infection in a short period of time, and from experimental evidence (Fairley[5]), from animals infested with large numbers of cercariae. Experimental animals heavily infested die before oviposition occurs.

The nature of this nocuous substance is not clearly established but the following facts are noted in evidence that it is the result of simple protein splitting rather than toxin production:

(*a*) Histologically there is abundant evidence of the digestion and removal of the embryos by the phagocytic cells of the body. This is attended by blood changes that are characterized by a mild to severe anemia of the secondary type, slight leucocytosis and a marked relative increase in the number of eosinophiles and large mononuclear cells (personal observation, and Day [2]).

(*b*) Much pigment similar to that deposited in malarial infections is deposited in the internal organs, particularly the spleen and liver. This pigment is similar in character to that seen in the enteric canal of the parasites.

(*c*) Fairley has shown that there is a specific reaction in the body that results in a constant (88 per cent) fixation of complement when extracts of the livers of infected snails are used as the antigen.

(*d*) Clinical experience does not indicate the formation of immunity in the patient even after he has been long infected.

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DESCRIPTION OF PLATES

PLATE 1

FIG. 1. Bilharzia parasite, male, in an interlobular vein of the liver. Note the large size of the vessel and the surrounding fibrous tissue.

FIG. 2. Bilharzia parasites, male and female, in the veins at the base of a rectal polyp. The male enfolds the female.

1

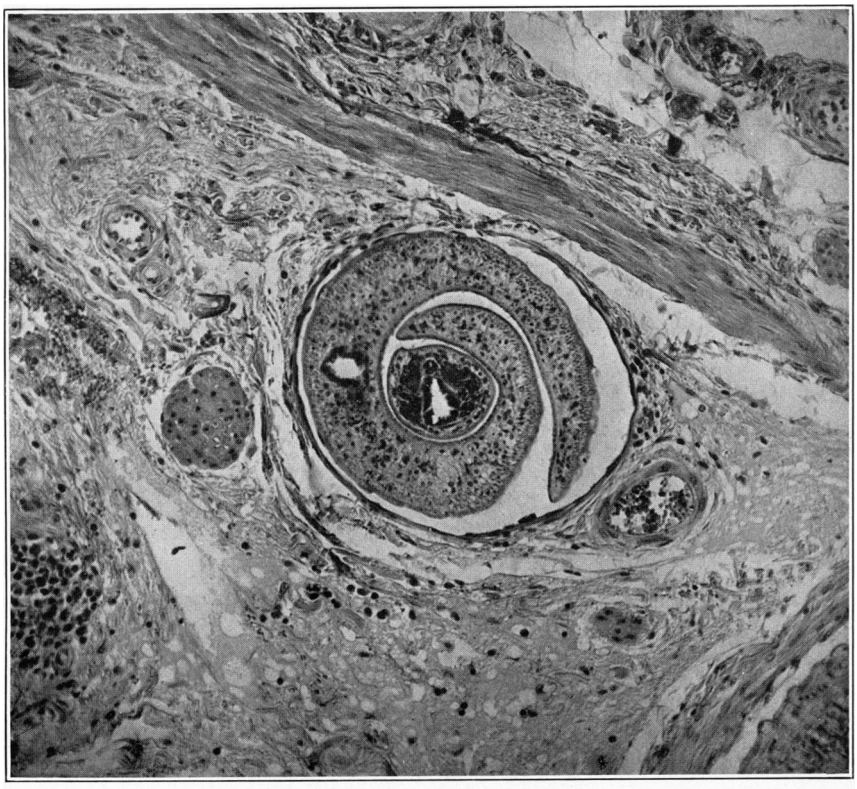

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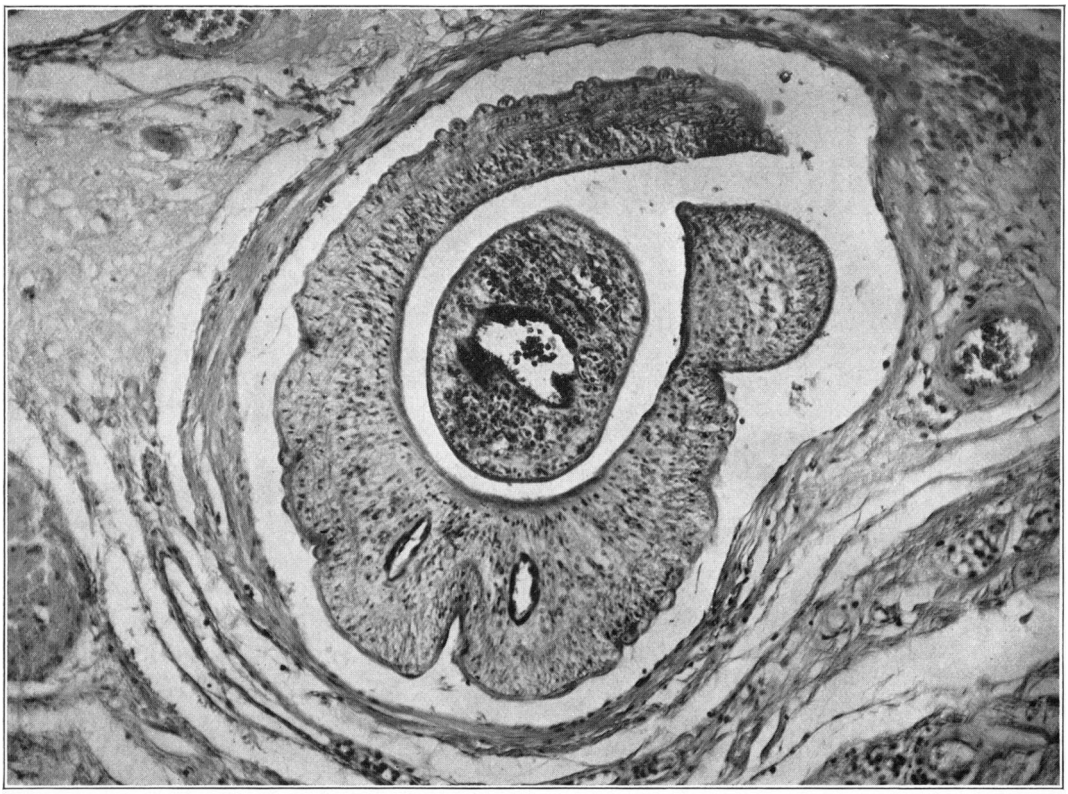
PLATE 2

FIG. 3. Bilharzia parasites, male and female; the cross-section taken posterior to the bifurcation of the intestinal canal of the male.

FIG. 4. Bilharzia parasites, male and female, in cross-section through the ovary of the female.



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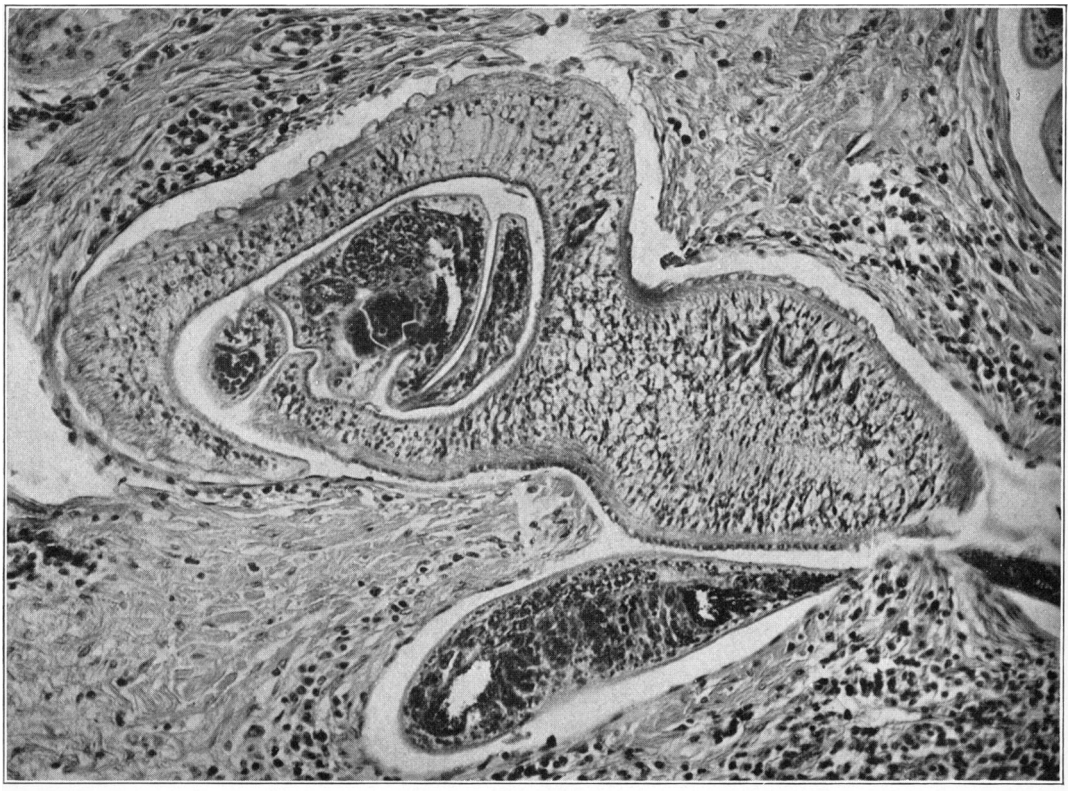


4

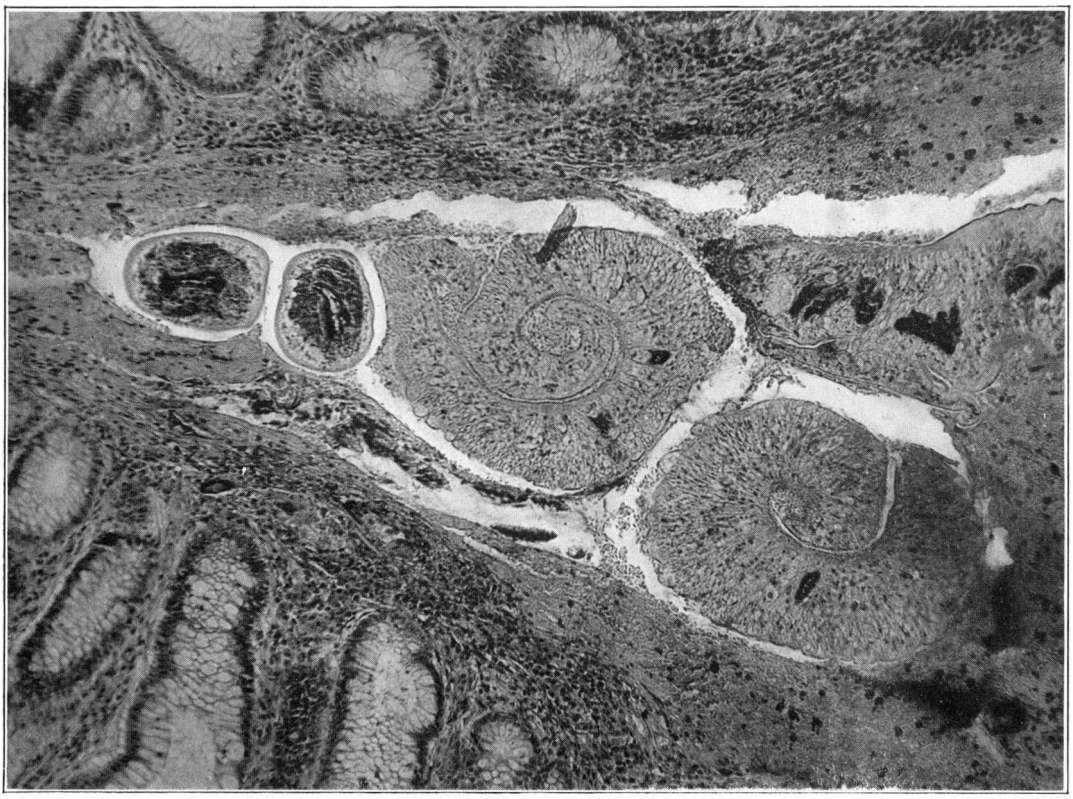
Hutchison Pathology of Bilharziasis

PLATE 3

FIG. 5. Bilharzia parasites, male and female. The females are not in the gynecaproic canal of the male.

FIG. 6. Bilharzia ovum, *S. mansoni*, from a rectal polyp, showing the surrounding inflammatory reaction. Many of the polymorphonuclear cells are eosinophiles.

FIG. 7. Bilharzia ovum, *S. mansoni*, in a rectal polyp. This ovum is dead and a giant cell has formed against its shell and within its lumen.



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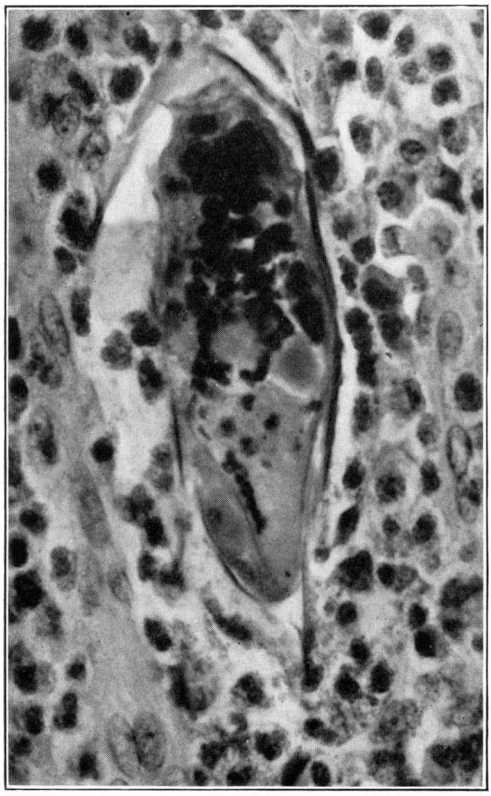

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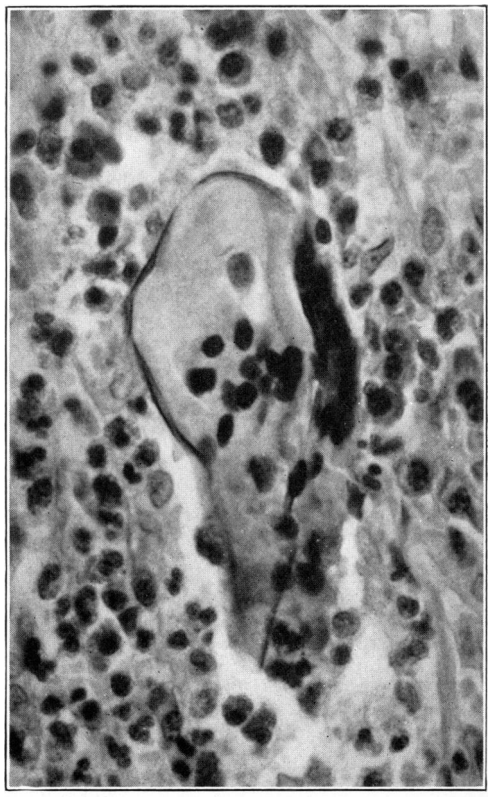

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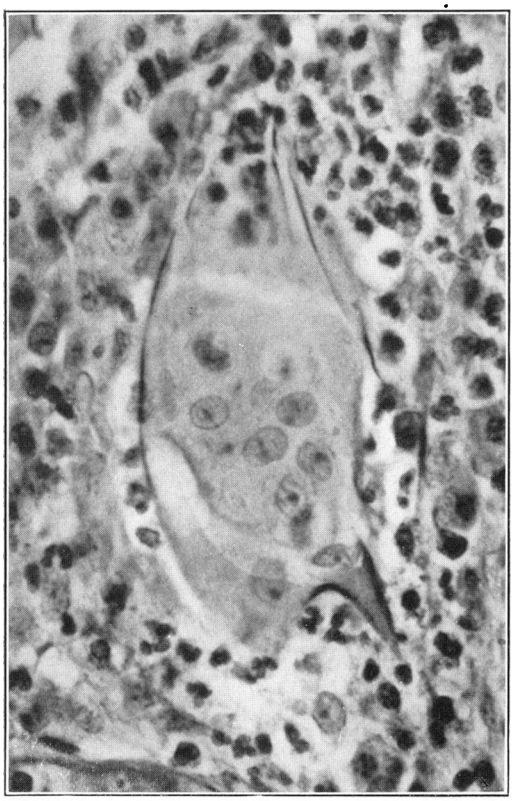
Hutchison Pathology of Bilharziasis

Plate 4

Fig. 8. Bilharzia ovum, *S. mansoni*, showing the lateral spine. The embryo is replaced by tissue cells.

Fig. 9. A very large giant cell about an empty ovum.

Fig. 10. Pseudotubercles about ova in the fat of an epiploic appendage.



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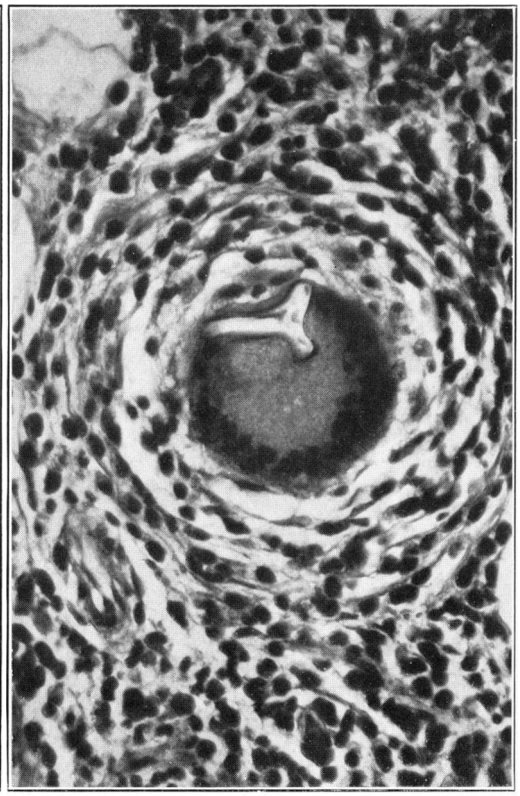

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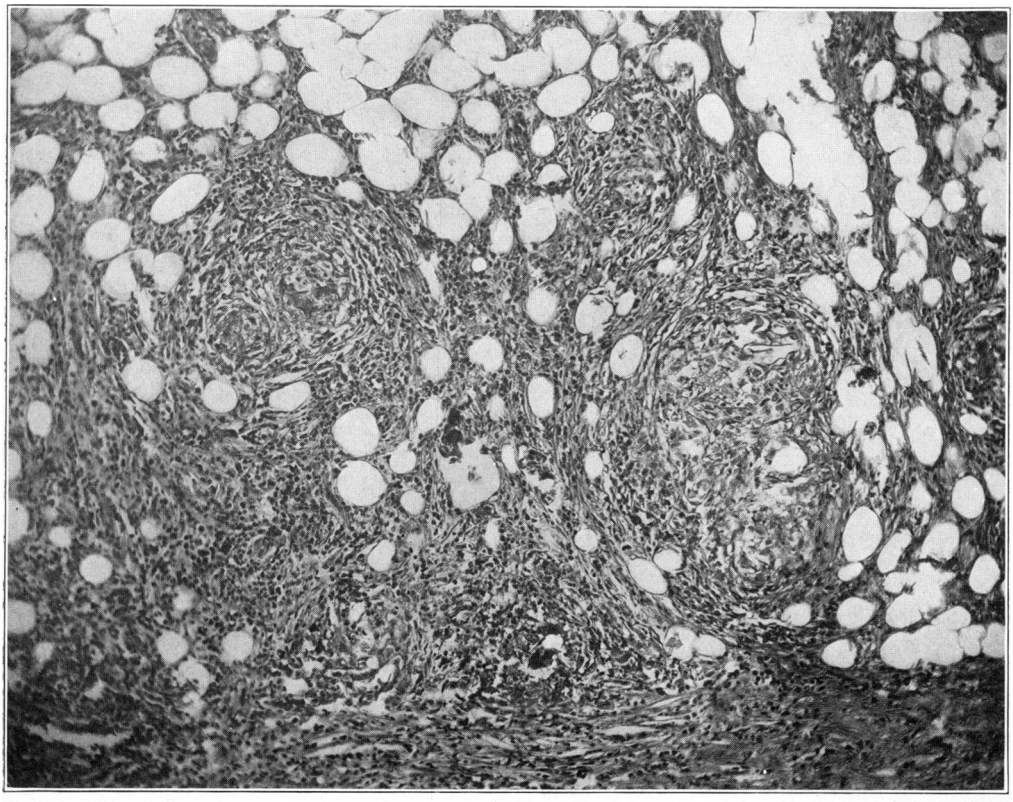


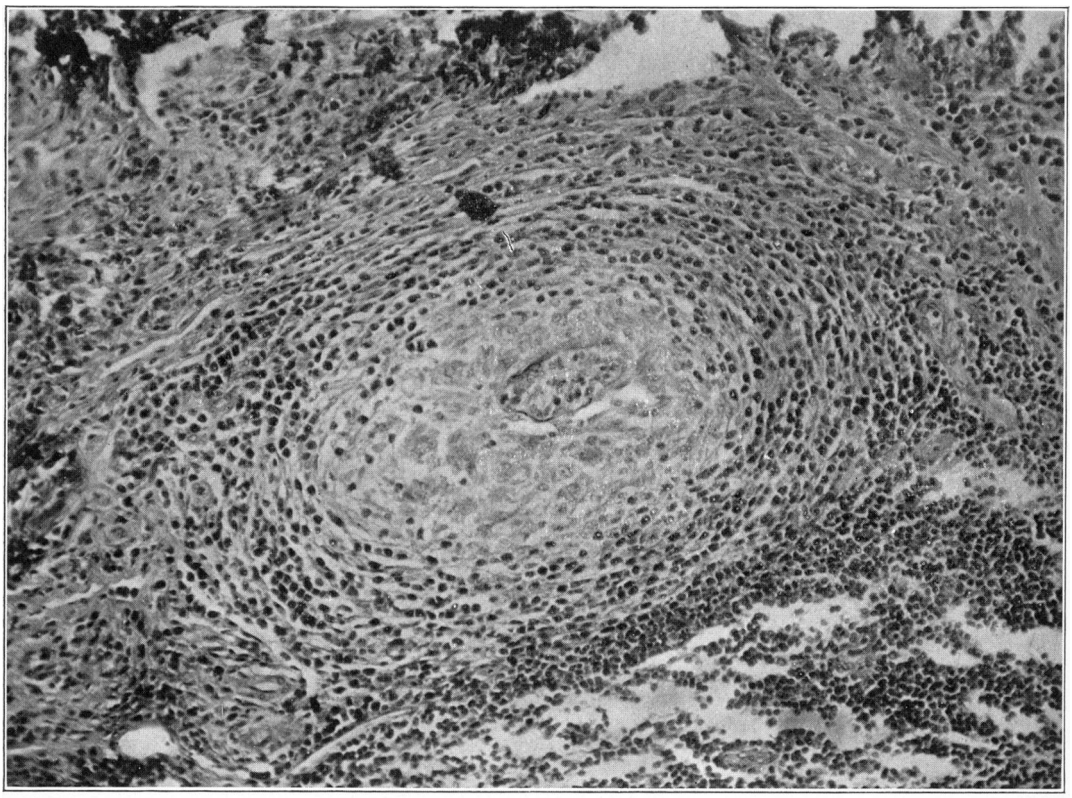
10

Hutchison Pathology of Bilharziasis

Plate 5

Fig. 11. Pseudotubercle, late stage, with marked formation of fibrous tissue.

Fig. 12. Bladder wall showing dense infiltration with ova of *S. hematobium*, many of which are calcified.



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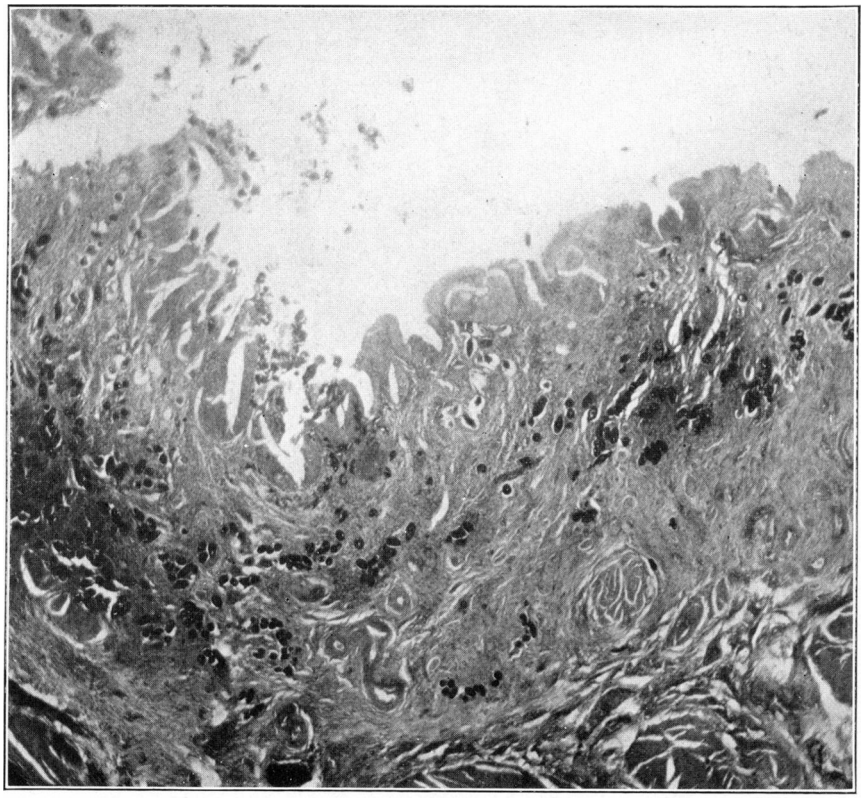

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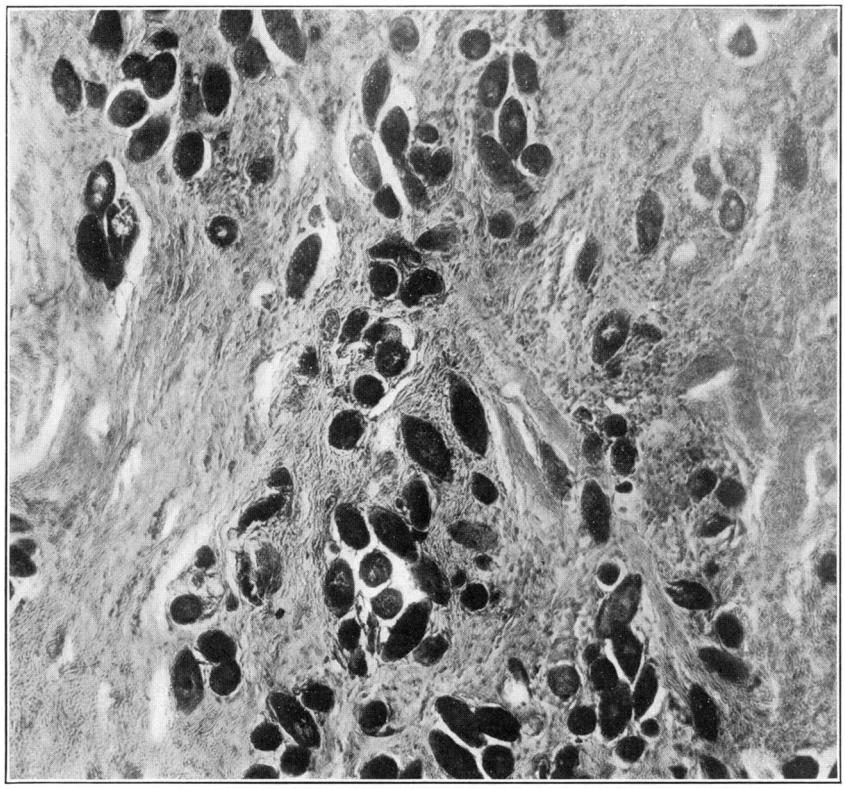
PLATE 6

FIG. 13. Terminal spined ova of *S. hematobium* in the bladder wall, (comparatively low magnification).

FIG. 14. Mucinous degeneration in the columnar epithelium on a rectal polyp. The dark spot under the mucosa is the cross-section of an ovum.



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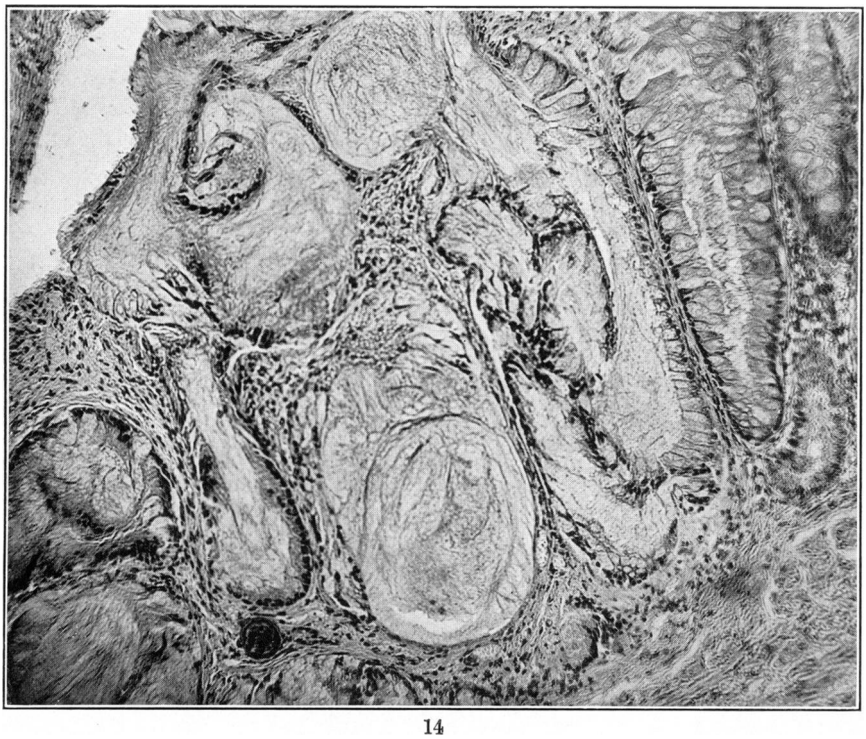

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