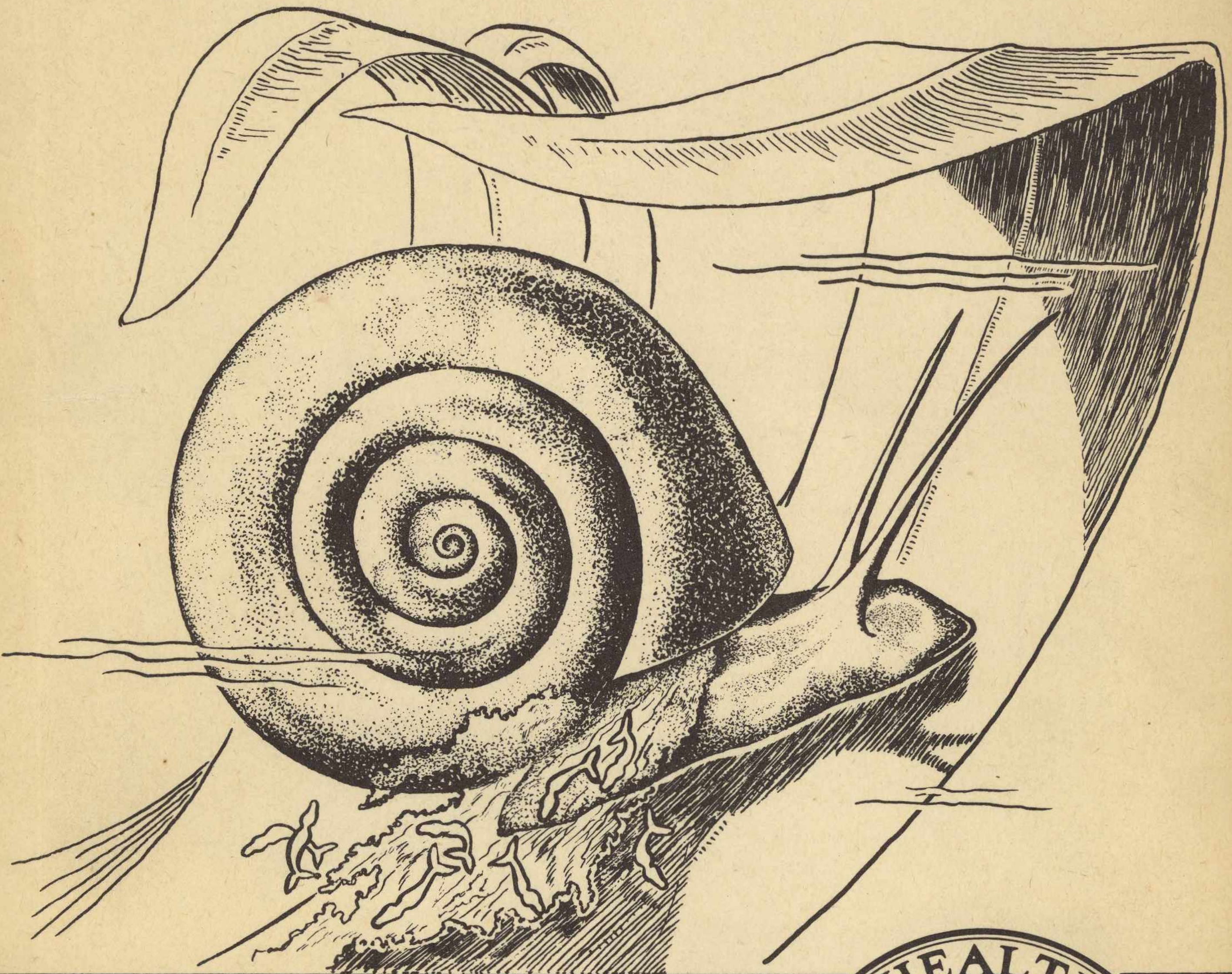
TROPICAL DISEASE SERIES

SCHISTOSOMIASIS



FEDERAL SECURITY AGENCY

U. S. PUBLIC HEALTH SERVICE

MALARIA CONTROL IN WAR AREAS

ATLANTA, GEORGIA MAY 1946

SCHISTOSOMIASIS

Tropical Disease Series

This manual is designed to accompany the film strip "Schistosomiasis" and contains supplemental information on the disease. The purpose of the film strip is to bring to the attention of physicians and health officers the clinical manifestations of schistosomiasis, the importance of early diagnosis and treatment of the disease and the possibility of spread of the disease to this country. The film strip and manual are productions of the Training Division and the Division of Laboratory Services, Office of Malaria Control in War Areas, U. S. Public Health Service.

DESCRIPTION OF THE FILM STRIP

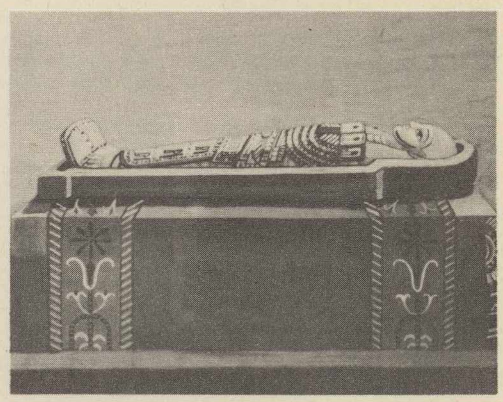
TITLE	:	Schistosomiasis.
PRODUCTION NUMBER	:	MCWA - TE - 5-006 - Ed. I.
SIZE AND TYPE	:	35 mm., color with sound.
RUNNING TIME	:	16 minutes.
CLASSIFICATION	:	A training film for practicing physicians.
AVAILABILITY	:	Training Division, M.C.W.A. U. S. Public Health Service 605 Volunteer Building, Atlanta, Georgia.

THE BLOOD FLUKE DISEASES

The endemic areas of schistosomiasis embrace thousands of square miles in Asia, Africa, and the American tropics. Some of the most densely populated areas in the world are involved, and a conservative estimate of the total numbers of people infected throughout the world might approach 20 to 25 million cases. It is typically an infection of rural and agricultural populations and is usually associated with agricultural or domestic habits which favor its spread. However, the disease is no respecter of persons or classes.

Schistosomiasis has been found in the mummies of Egypt as early as 1250 B.C. Ruffer, in 1910, conducted histological examinations of some of the Egyptian mummies of the 20th dynasty (1250-1000 B.C.) and discovered schistosome ova among the straight tubules of the kidneys. These observations have since been confirmed by several investigators. Undoubtedly, the disease dates back a considerable length of time before the 20th dynasty, but these are the earliest known records. The Egyptian papyri from as early as 3000 B.C. discuss hematuria and contain prescriptions which are obviously intended for the cure of the clinical disease.

One of the more recent historical evidences of the disease is in the reports that the French troops engaged in the Napoleonic Campaigns in Egypt in 1700-1801 suffered severely from hematuria, a clinical manifestation of one of the blood fluke infections.

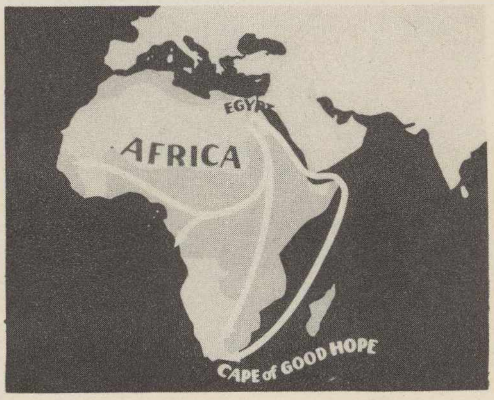


The evidences of the infection in the early relics of the Egyptian civilization would indicate that the human disease may perhaps have originated there. For thousands of years the agricultural practices in the lower Nile valley and its delta have been favorable to the spread of the disease and today this area composes the greatest center of endemicity for both *Schistosoma mansoni* and *S. hematobium*.

The etiology of the disease was first discovered by Bilharz in 1851, and he later established the relation between the blood flukes and the hematuria, dysentery, and pathological lesions which were so common in Egypt. The two species of blood fluke present in Egypt were not differentiated until the work of Sambon in 1907, and the full life cycle was not fully demonstrated until 1915.

The bladder vessel fluke, *Schistosoma hematobium*, has been spread westward along the Mediterranean in Africa, and to Portugal. North and East it has spread to Cyprus, Palestine, Arabia and Iraq.

An ideal situation existed for the spread of the blood flukes throughout the Mediterranean region and the African continent. The spread of *S. hematobium* through the Mediterranean region and Asia Minor has been amply provided for by the early Egyptian wars of conquest, the aggressive trade of the Phoenicians, the conquests of Alexander and his heirs, the Roman conquests, and the later arrival of the British and French with their railroads and maritime commerce.



Southward the disease has extended down the East Coast to the Cape of Good Hope and across Central Africa to the West Coast.

The spread of the disease through the African continent to the South and West was undoubtedly accomplished by the aggressive intra-continental slave trade which was indulged in by many of the tribes throughout Africa and by the more civilized peoples of the North.

One of the mesenteric blood flukes, *Schistosoma mansoni*, has spread from Egypt south to the Transvaal and west to Gambia.

Schistosoma mansoni was carried to the American Tropics in the bodies of negroes destined to work the plantations.

The archeological basis for the belief that the infection was brought to this country by the slaves is the complete absence in the native American records of any pathological descriptions typical of *S. mansoni* infections. During the 18th century an extremely large number of slaves was brought to the Americas, the largest part of them being distributed throughout the tropical or semitropical regions. The infected slaves were probably brought from the Congo Basin and Angola on the West Coast of Africa, as well as from the Kaffir lands (Mozambique, Zululand, and Basutoland) on the Southeast coast.

Through the slaves schistosomiasis was seeded into the peoples of Puerto Rico and the Lesser Antilles, of Venezuela, Brazil, and the Guianas.

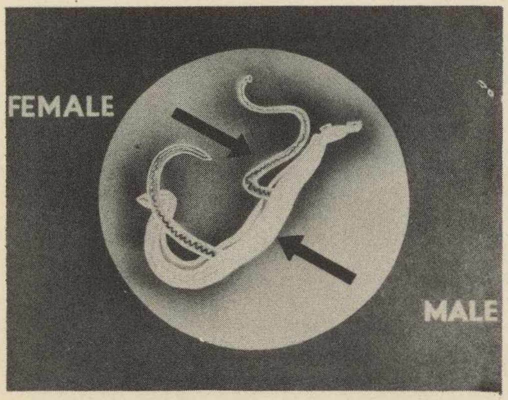
Schistosomiasis was first noted in the Americas in 1904 by Dr. Gonzalez Martinez when several Puerto Rican cases were discovered. The disease was discovered in Venezuela in 1906, and is now known to be present in the Lesser Antilles, Brazil, and the Guianas as well. Autochthonous cases have not as yet been described from North or Central America, British Guiana, Colombia, or islands of the Caribbean outside of the Lesser Antilles. Perhaps the greatest areas of endemicity in the New World are in Puerto Rico and Venezuela.

S. hematobium has never appeared in the Americas, perhaps because of the absence of a susceptible intermediate host.

Although Schistosomiasis is widely distributed in the Orient, there the great pool of human cases is in the lower Yangtze Valley in China. Here the disease is caused by *S. japonicum*, another mesenteric blood fluke.

Oriental schistosomiasis is probably as old as the Egyptian infection although the earliest recorded account of the disease was by Fujii in 1847, and the causative organism was not discovered and named until 1904 by Katsurada. The intermediate host cycle of the parasite was established by Miyairi and Suzuki in 1913-14.

In addition to the Yangtze, other endemic areas in China include coastal areas, Shiuchow (near Canton), Foochow, the Mekong Valley, and the Burmese Border. Five endemic foci exist in Japan; it is especially prevalent in the province of Hiroshima and in the village of Katayama. The infection is also found in Formosa, the southern Philippines, and in the Celebes.



Unlike all other flukes, the sexes are separate in schistosome worms. The female is usually found clasped lengthwise within the grooved body of the male.

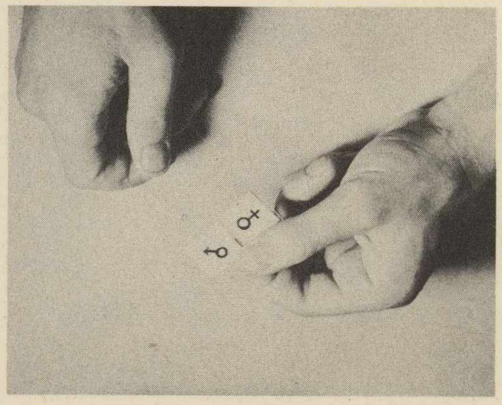
The body of the male worm is characteristically widened and infolded behind the ventral sucker, forming the so-called gynaecophoric canal in which the female is held at the time of copulation. The light gray or whitish male varies from 6.4 mm. to 20 mm. in length, according to the species.

The darker female worms are cylindrical and pointed at each end and vary from 7.2 mm. to 26 mm. in length according to the species. The middle portion of the female is usually held within the gynaecorphoric canal of the male, the anterior and posterior portions being free.

The mature worms are about the size of small pins.

The adults of the three species may be differentiated by several features:

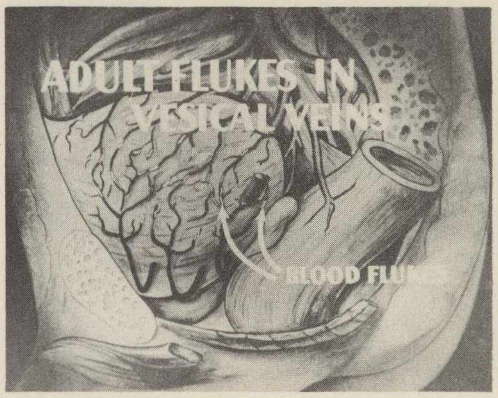
1. *S. hematobium* - Male: 10-15 mm. long by 0.8-1 mm. wide; cuticula finely tuberculated; four large testes. Female: 20 mm. long by 0.25 mm. wide; uterus long and voluminous, contains about 20 eggs.
2. *S. mansoni* - Male: 6.4-9.9 mm. long by 1.1 mm. wide; cuticula grossly tuberculated; eight small testes. Female: 7.2-14 mm. long by .16 mm. wide; uterus short, contains 1-3 eggs.
3. *S. japonicum* - Male: 12-20 mm. long by 0.5-0.55 mm. wide; cuticula smooth; 7-8 slightly lobate testes. Female: 12-26 mm. long by 0.3 mm. wide; uterus well developdd, contains 50 to 300 eggs.

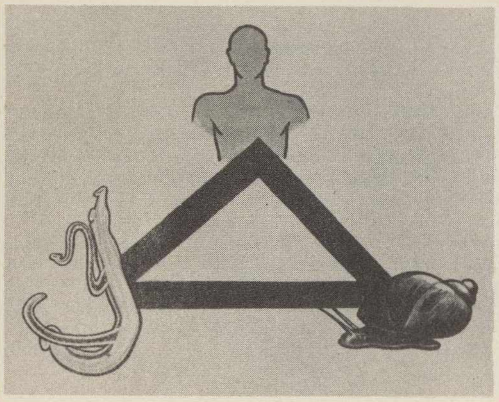


All the schistosomes are parasites of the venous system of their final host. *S. japonicum* and *S. mansoni* adults are usually found in the superior and inferior mesenteric veins, the hemorrhoidal plexus, and the portal system.

In massive infections where the worms are crowded out of their normal environment the adults may be found in any organ of the body, the lungs and liver being favorite sites for the displaced worms. Even in light infections the adult worms are occasionally found in locations other than normal.

The adults of *S. hematobium* may inhabit any of the veins or venules of the pelvic region, but are most commonly found in the vesical veins, the vesicoprostatic, the pubic and uterine plexuses, and less commonly in the mesenteric branches of the portal vein. In this species also, the worms may migrate to any vein or organ in the body when massive infection and over-crowding occurs.



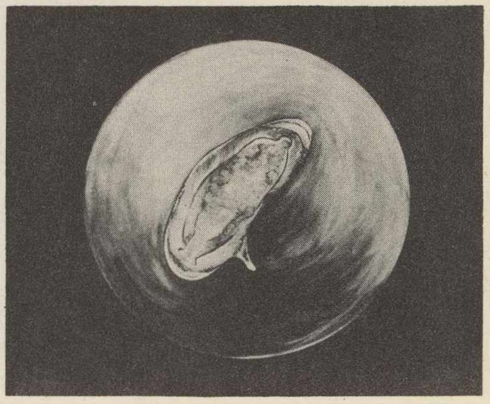


Eggs are passed via the urine and feces. Snails are infected with the larval stages. Larvae breaking forth from the snails attack men to complete the triangle of the blood flukes and their two hosts.

Only snails of certain species are able to act as intermediate hosts, and these hosts are also specific for each species of parasite. Several species of *Bulinus*, *Physopsis* and *Planorbis* are hosts for *S. hematobium* and *S. mansoni* in Egypt and other parts of Africa, while in the New World *Australorbis glabratus* is the intermediate host for *S. mansoni*. Certain species of *Katayama*, *Oncomelania (Blanfordia)*, and *Schistosomophora* are the principal intermediate hosts of *S. japonicum* in the Orient.

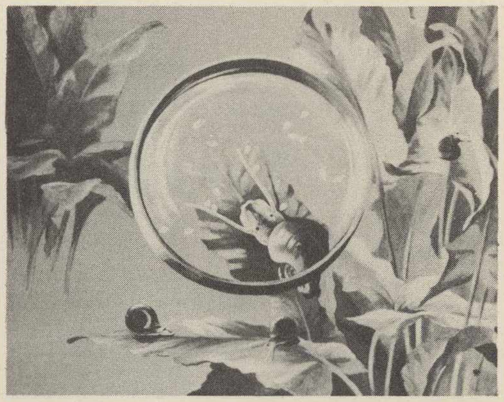
Man is the principal definitive host, but monkeys are also the natural hosts of *S. hematobium* and *S. mansoni*, and dogs, cats, cattle, horses, and hogs serve as natural hosts of *S. japonicum*. All species may be transmitted with comparative ease to laboratory animals.

The egg, as found in the feces or urine, usually contains a mature or nearly mature miracidum. This larval form generally emerges from the egg 2 to 16 hours after its original medium is diluted with water. Hatching will take place under rather wide limits of temperature and is brought about through various internal and external factors, such as the hypotonicity of the water and the activity of the larva. The unhatched eggs can survive less than 24 hours in putrefying feces, but may remain viable for a week in formed feces at a lower temperature.



In hatching, the miracidium emerges through a longitudinal split in the shell and almost immediately begins its very active free-living existence. The miracidum is an oval, pyriform, ciliated organism with a cone-shaped anterior. The internal organs consist of a primitive digestive tract, anterior and lateral paired penetration glands, primitive excretory and nervous systems, and a posterior mass of germinal cells. The larvae range from 97 to 140 microns long by 35 to 66 microns wide, according to the species. By means of the cilia the larva swims very rapidly in a straight course, avoiding obstacles, usually within a very few centimeters of the surface. The miracidium is positively phototropic, negatively geotropic, and is positively attracted to its specific mollusc host, probably through the exudates of the snail. The infective stage of the miracidium is only 60 to 72 hours, after which it sinks to the bottom and dies.

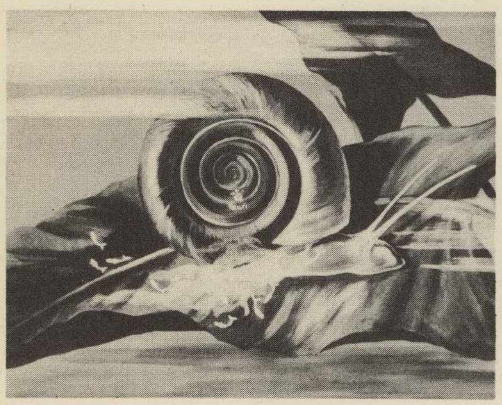
Within a short time after contacting the suitable snail the larva attacks and penetrates the part with which it first came in contact, usually the tentacles, head, foot, or mantle cavity. Infection of the snails usually takes place in the upper few centimeters of water, the position most frequently occupied by both the snail and the parasite. Penetration of the snail is brought about by a combination of a head-on boring action and the secretion of supposedly proteolytic substances from the secretory glands of the miracidium.



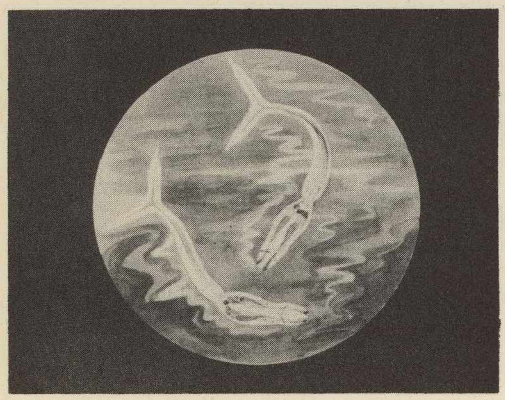
During the next few weeks the larva continues its migration through the body of the snail, assuming an elongate, sac-like appearance, and by the fifth week it has definitely differentiated into a primary sporocyst, about 400 microns in length, and containing elongating secondary sporocysts. By the sixth week practically all the worms have reached the lymph spaces between the liver and gonads and most of the primary sporocysts have ruptured, setting free the secondary sporocysts.

Only a few secondary sporocysts arise from each primary sporocyst, and these contain the germ-balls of the cercarial generation. Most of the secondary sporocysts are located in the lymph spaces and interstices in and around the digestive gland (liver) of the snail.

The most critical period for both the snail host and the cercariae is when these rapidly maturing forms rupture the sporocysts and escape, sometimes with enough tissue damage to kill the snail host. Thousands of cercariae are produced by a single second-generation sporocyst. A single miracidium may produce as many as 200,000 cercariae.

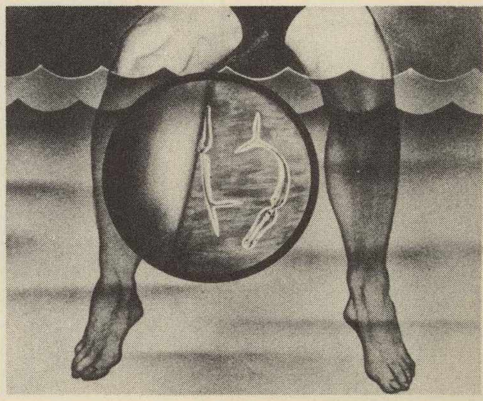


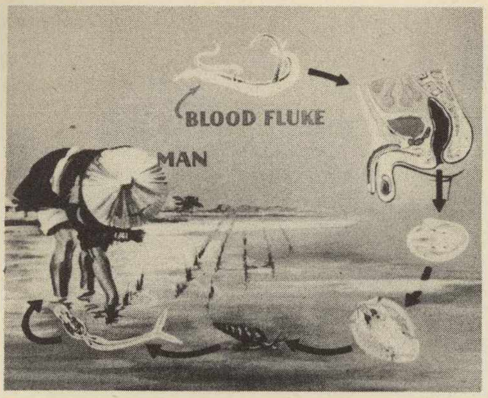
The mature cercaria has an elongate pear-shaped body and a long terminally forked tail. The body measures 140-240 microns long by 57-100 microns wide. The tail consists of a trunk (175-250 microns by 35-50 microns) and a pair of caudal furci (60-100 microns long). The cuticle of the body and tail is covered with minute backward-pointing spines. There is a large urn-shaped anterior sucker and a smaller discoid ventral sucker, and the great mass of the body is filled with five pairs of lytic or penetrating glands.



The cercaria moves tail first through the water at all levels, rising and sinking and using the caudal furci as anterior propellers. It spends much of its time attached to the surface of the water by means of the ventral sucker. The viable life of the cercaria is about 24-30 hours, during which time it must penetrate a mammalian host to continue existence.

When the cercaria encounters a warm blooded host it attaches itself to the skin by means of the ventral sucker. It is thought that the cercaria is stimulated to enter the skin when the host leaves the water and drying of the affected part is initiated. Penetration is effected by the forceful ramming of the anterior end of the cercaria into the skin, accompanied by the digestive action of the liquids poured out by the penetration glands. Penetration through the outer epidermis generally takes less than one-half hour. Usually within 24 hours the larvae have worked their way through the skin and gained access to the superficial venules, where they begin their migratory tour of the final host.

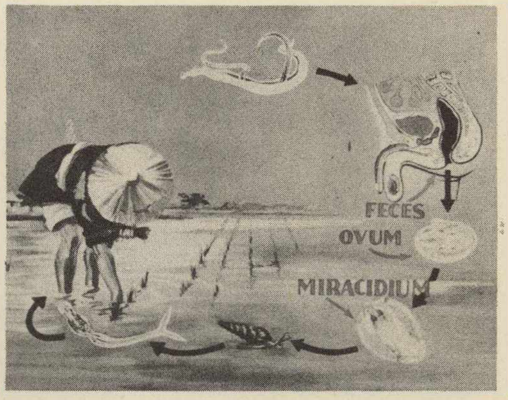




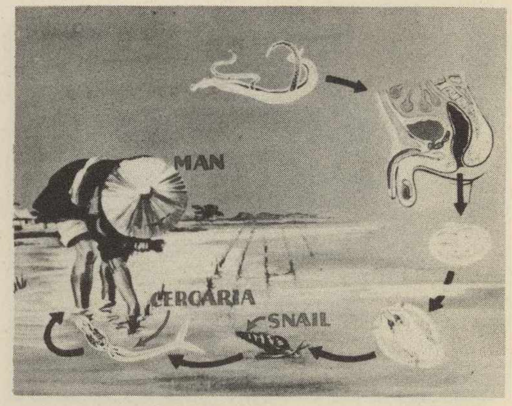
The life cycle of the blood flukes is a marvel of biology. Man or other mammals are the definitive hosts; here the adult blood flukes localize in mesenteric and bladder veins.

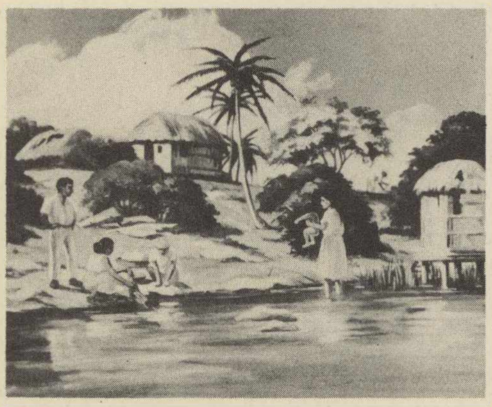
It can be seen that the parasite can only survive and spread from final host to final host through a very specific combination of events and conditions. The extra-mammalian cycle must be initiated by pollution of water with the eggs in the urine or feces of any infected man or other mammal.

The miracidium must find a susceptible species of snail in which to carry on the life cycle and provide for multiplication of the parasite. After completing the development in the snail the cercaria again must seek out a susceptible final host which is present in the parasite's environment.

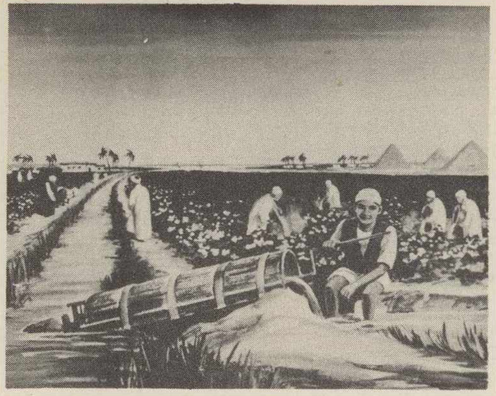


This system of two hosts is a marvel of parasitic adaptation designed primarily for the increase of animal numbers, and thus increasing the chances of completing the life cycle. It is perhaps this very efficient system of asexual reproduction which has made possible the high rate of incidence of the disease in many endemic centers. However, it is also this complicated chain of events in the parasite's life history which makes possible the intervention of man in preventing the completion of the life cycle. A break at any point in the chain will control the spread of infection. The removal of the source of infection, the removal of the specific snail host, or the protection of the susceptible final host would all be effective measures, though none of them are as yet practicable in the worst endemic centers of this disease.





Schistosomiasis is widely distributed throughout Puerto Rico and is an important health problem there. It has been estimated that up to 12% of the population are infected. The two types of environment responsible are the streams and pools, used for bathing and other domestic purposes, and the irrigation system. The intermediate host, *Australorbis glabratus*, prefers quiet waters of stream pools, irrigation ditches, and reservoirs. The habits of the people play an all-important role in the spread of the infection. The natives commonly use the snail-infested waters for bathing and washing and there is excessive human pollution of the water and diversion of untreated sewage into streams.



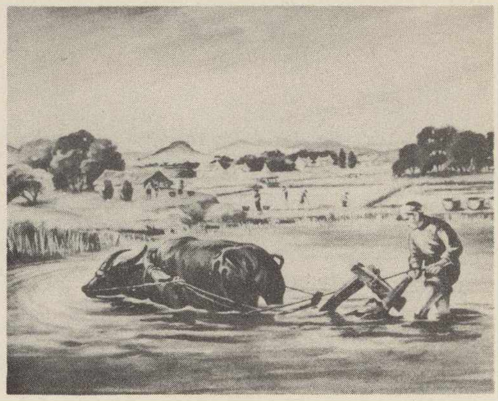
Scott (1939) has estimated that at least 6 million of twelve million rural inhabitants of Egypt are infected with *S. hematobium*, 3 million have *S. mansoni* and at least 1-½ million have both species. In some areas 85% are infected with one or both species, and as high as 22 deaths per 1000 population are recorded as due to schistosomiasis in some foci.

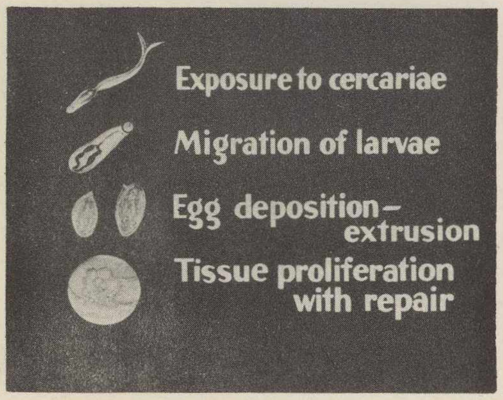
The people of the Nile Delta and lower valley live and work within a vast maze of irrigation canals and ditches. These are generally infested with the proper intermediate hosts and human pollution of these waterways is extremely common. A Mohammedan religious custom, demanding bodily cleansing following defecation, leads to almost invariable pollution of water, as well as exposing the subject to infection.

The intermediate host for *S. hematobium* in Egypt is the snail *Bulinus truncatus*. *Planorbis boissyi* acts as the intermediate host for *S. mansoni* in Egypt.

Faust and Meleney (1924) estimate that tens of millions of Chinese are exposed yearly to infection with *S. japonicum*. The incidence in some areas is as high as 95% and ranges from 1% on up, throughout the endemic centers. Altogether thousands of square miles in China are involved in these endemic foci, with a population of 100 million people, of which some 10% are estimated to be suffering from active infections. The intermediate hosts in China are the snails *Oncomelania hupensis* in the Yangtse Valley and *Katayama nosophora* along the Chinese coast.

These snails are present in the vast number of flooded rice fields, irrigation ditches and reservoirs. The habits of the natives in their agricultural and domestic pursuits leads to ample pollution of the water and infective contact with it. The use of human excrement as fertilizer in the rice fields is also extremely important in maintaining the disease in China.





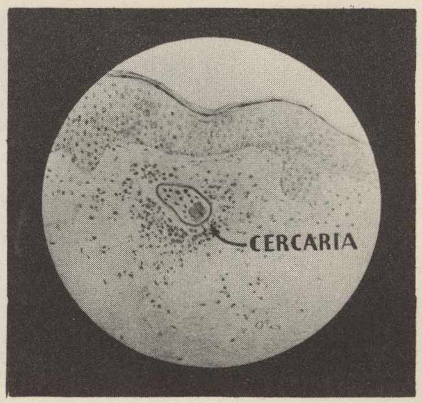
Clinical manifestations fall into four phases: the phase of *exposure* to the cercariae; the phase of *migration* of the developing worms; the phase of maturity of the adult worms with *egg deposition* and *egg extrusion* from the body; the phase of continuing infection, and *tissue proliferation* with *repair*.

In nature in the endemic areas there would usually be an overlapping of these stages due to successive infections from continuous exposure over a long period of time.

Cercerial penetration of the skin may give rise to a more or less intense local reaction in the form of red, slightly raised, pin-point-sized petechiae, developing within a very few hours after the entry. A definite tissue reaction can be seen in the skin at the points of entry. This consists of edema, a moderately dense accumulation of wandering cells, and congestion of neighboring capillaries. The reaction reaches a maximum in 24 to 36 hours and disappears in 3 to 4 days with a transitory adenitis of the local superficial lymph glands.

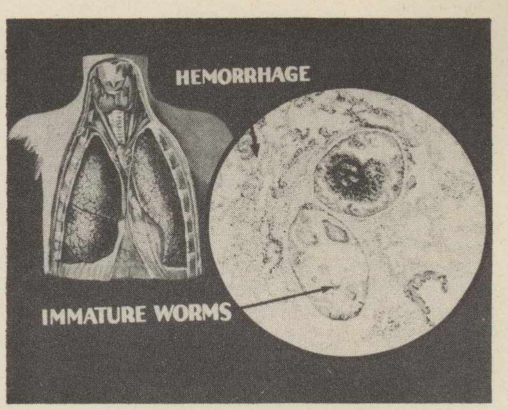
In several areas in this country man is subject to a more severe dermatitis caused by penetration of various cercariae of Strigeid flukes which naturally infect birds, mice, etc. The resistance of man as an abnormal host explains the severe reaction. Man acquires this so-called "swimmer's itch" by the invasion of cercariae while swimming or wading in snail-infested waters.

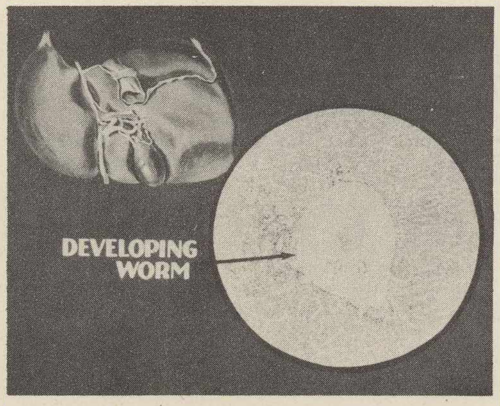
Individuals vary in their reaction to cercarial invasion of both types. Some show very definite and severe pathology, while others are not visibly affected.



The immature worms find their way to the veins and are carried to the lungs; this requires two or three weeks.

The symptoms of this stage are not very pronounced and may be absent entirely in light infections. In experimental infections of mice and dogs the pathological picture is quite clear. The most conspicuous feature is the alveolar hemorrhage, with an intense congestion of the blood capillaries in the alveolar walls and of the larger vessels. Another prominent feature is edema of the spaces surrounding the larger blood vessels. In some of these spaces are seen dense accumulations of white blood cells.



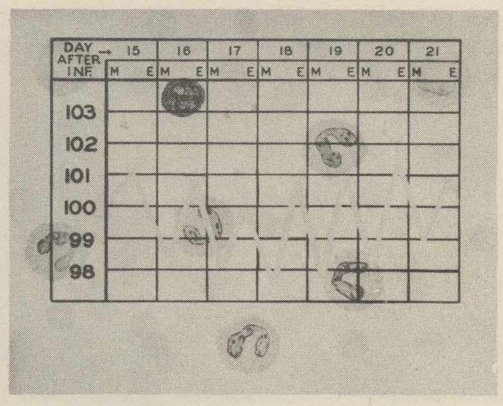


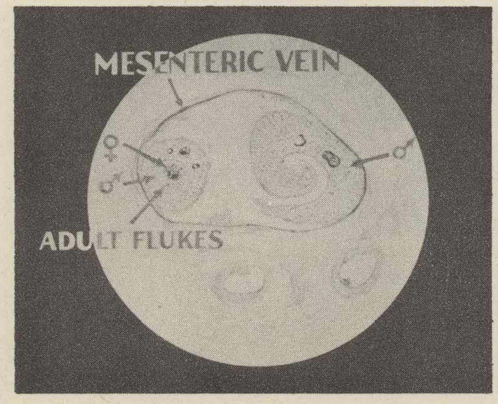
From the lungs the developing worms find their way to the liver lobules. Nausea, vomiting, headache, and abdominal pain may be the systemic complaints.

It has been possible to work out the route of migration of the parasites from the lungs to the liver through the use of experimental animals. The young worms are carried in the blood from the lungs to the heart and from there to the systemic circulation. The majority are shunted into the abdominal aorta, and those which reach the mesenteric or coeliac artery pass through the mesenteric capillaries into the portal circulation and are carried to the liver. Here the immature worms feed and grow, become sexually differentiated and, upon reaching adolescence, move out of the liver against the current of incoming blood.

Urticaria may occur. Leucocytosis is considerable, and very marked eosinophilia is frequent. Fever runs a remittent course.

The pathology of this period of maturation is negligible, except in cases of massive infection, although the apparent symptoms may be severe. It is probable that the symptoms seen during the migratory and growth stages are due to a general systemic reaction to the toxic products of the worms, or are those of a typical allergic response. In extremely heavy infections toxins secreted by the worms apparently produce a necrosis of the liver parenchyma and a degeneration of the convoluted tubules of the kidneys.

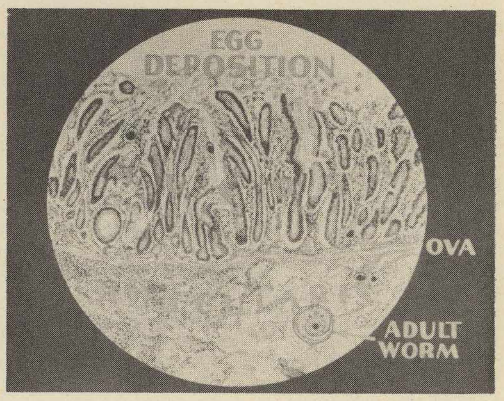


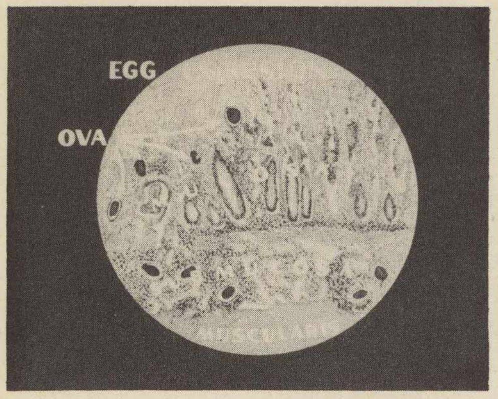


After becoming nearly mature in the liver the worms migrate against the blood stream to the small veins of the mesenteries or vesical plexus, depending on the species. *S. mansoni* is usually found in the mesenteric venules draining the colon and the terminal section of the small intestine. The typical habitat for the *S. japonicum* adults is the radicles of the superior mesenteric vein draining the small intestine. *S. hematobium* adults migrate to the small venules of the bladder, rectum or other pelvic organs. During their migration the adults become sexually mature and copulation may take place en route. Egg deposition begins when the mature worms reach the small venules of the intestinal wall or the bladder.

The adults of themselves seem to produce virtually no pathologic process in the mesenteric or other venules. They feed on serum and cells but not so gluttonously as to create any noticeable effect.

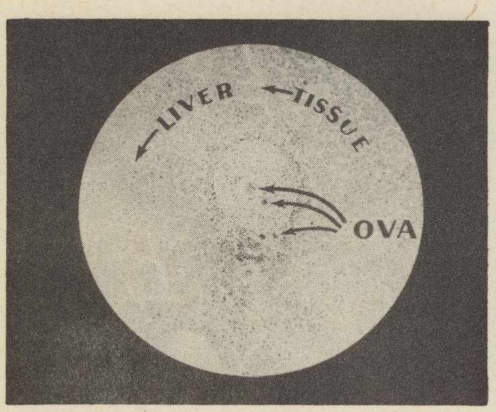
Egg deposition is initiated within an average of ten weeks following infection. The female mesenteric fluke, either in copula with the male or entirely in advance of the male, migrates to the venules in the submucosa or the mucosa of the intestine and deposits her eggs one at a time, backing out of the venule and moving to a new site when the venule becomes filled with eggs. This process may continue for a number of years. The eggs are at first easily passed through the intestinal wall into the lumen. This is brought about by pressure within the venule, the probable action of the spine and the more probable action of the lytic substances produced by the miracidium and passed through the egg-shell pores. As the egg extrusion continues the thickening of the wall and scar-tissue formation impede the progress of the egg and more of them are filtered out in the intestinal wall, walled off, and absorbed.





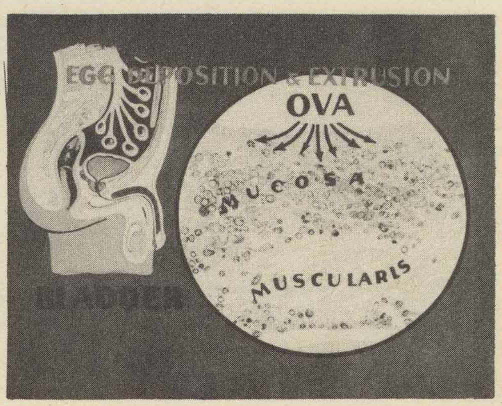
Abdominal pain, tenesmus, dysentery, bloodflecked stools, and remittent fever are the result of the intestinal process.

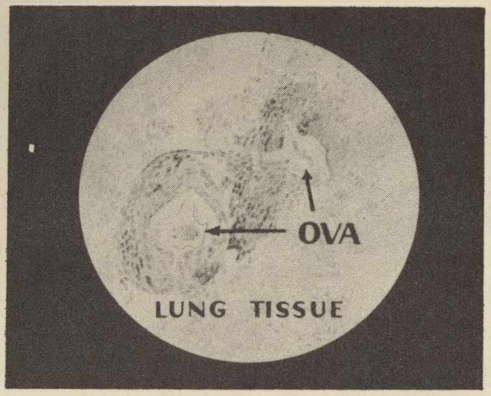
The pathological basis for the signs and symptoms evident in this stage is the development of abscesses and pseudo-tubercles around the infiltered and entrapped eggs in the tissues of the intestinal wall, as well as in the periportal tissues of the liver (described below). These abscesses frequently break through the intestinal wall and discharge their contents. Repair occurs with scar-tissue formation, and fibrous nodules develop in the pseudo-tubercles.



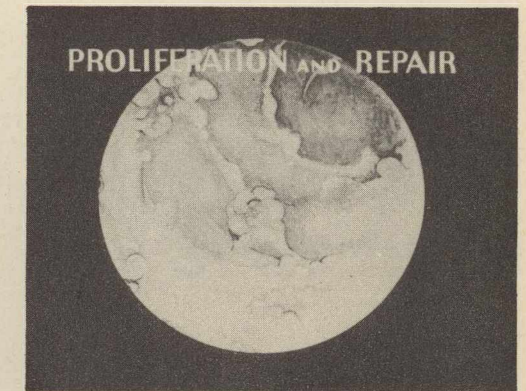
The involvement of the liver is due to the drift of eggs back through the portal blood stream into the liver and to their filtering into the periportal tissues, where they become centers of tissue reaction leading to hepatic cirrhosis. The liver becomes enlarged as a result of miliary abscesses around the infiltrated eggs and may be tender. At the same time the spleen becomes greatly enlarged. These changes are generally more pronounced in *S. japonicum* infections than in *S. mansoni*, probably because the daily out-put of eggs is greater in the former and because of the greater proximity of the worms to the liver in the superior mesenteric venules. Undoubtedly also the spine and the size of the *S. mansoni* egg tend to prevent it from drifting as easily as the egg of *S. japonicum*.

Deposition and extrusion of the eggs of *S. hematobium* usually takes place in the bladder mucosa or submucosa and is less commonly found in adjacent urinary and genital organs or the rectum. After being deposited in the venules, the eggs, aided by their own lytic secretions and spines and by surrounding tissue pressure, are able to escape to the perivascular tissues and filter out into the lumen of the organ, accompanied by blood and necrotic tissue cells. Later, eggs are more commonly held in the perivascular tissues and are the centers of abscess formation there. Some of these are able to break into the organ lumen and discharge the eggs, but the majority proceed to fibrosis, with resultant miliary pseudo-tubercle formation. Eventually the whole organ may become fibrotic, with phosphatic deposits in the mucosa and on its surface. Suprapubic tenderness, cysto-urethritis, and a mild remittant fever may be sequelae and hematuria is common.



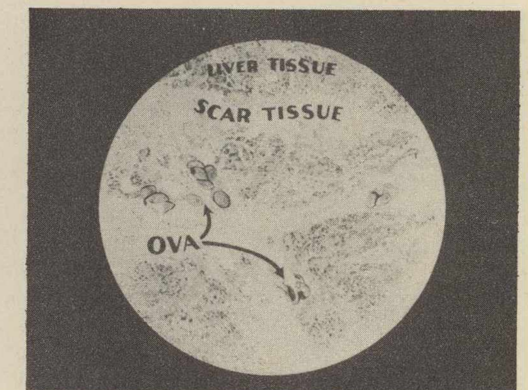


The eggs of *S. hematobium* may escape from the venules and drift back through the hypogastric and the common iliac veins, inferior vena cava, and the right heart to the lungs, where they are filtered out in the capillaries and cause a chronic inflammation. The eggs of this species also may drift back through the portal system to the liver, where they cause lesions similar to those resulting from eggs of the other species.

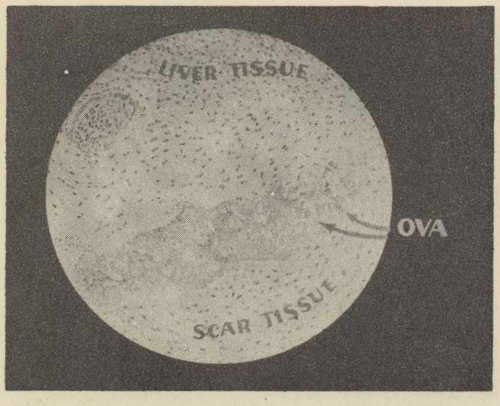


As infection continues, there is cumulative damage to the tissues of intestines, liver, bladder, and lungs. In the intestine there may be chronic proliferative colitis, papilloma formation, fistula development, with intermittent diarrhea as symptomatic evidence.

Fibrosis and thickening of the intestinal wall continue and progress until termination of the infection. The tone of the wall decreases and encroachment on the lumen by fibrous constrictions is evident. Secondary infection is an almost inevitable sequela to this intestinal involvement.



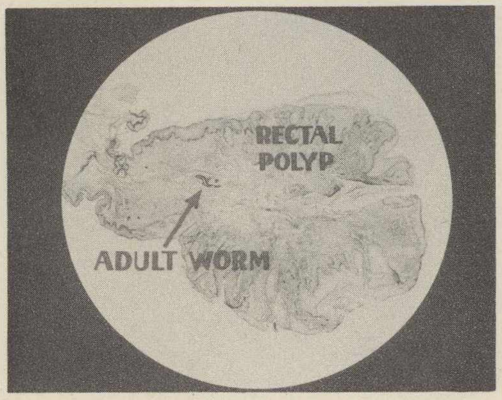
Because of the large numbers of eggs deposited in the liver, cirrhosis develops rapidly in *S. japonicum* infections. In *S. mansoni* infections the eggs are deposited slowly over a long period of time with the formation first of pseudo-tubercles and later a peculiar coarse cirrhosis, "pipe-stem cirrhosis", which consists of irregularly scattered white bands of connective tissue surrounding the large portal vessels. This same type of cirrhosis may be seen as a more rapidly developing process in *S. japonicum* infections.



Severe liver damage is typical. Pigment is often evident in the liver and spleen and is probably derived from blood ingested and digested by the adult worms. It is phagocytized by the endothelial cells and is indistinguishable from malaria pigment.

Ascites is an important sequela in the advanced stages of cirrhosis. This results from thickening of the large veins of the liver and periportal fibrosis, although it may be prevented, even in severe cases, by compensatory dilatation of the collateral circulation.

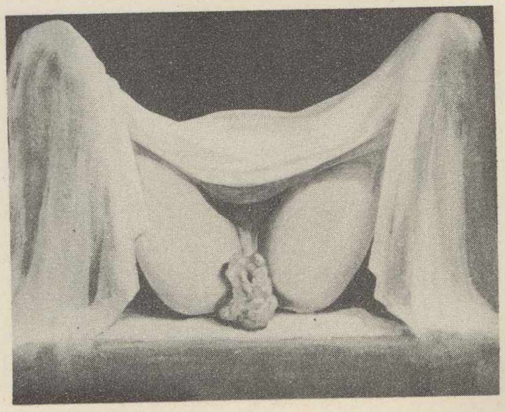
Splenomegaly commonly accompanies liver involvement and is attributed to a passive congestion. The spleen becomes congested, its fibrous reticulum increases and consequently it becomes greatly enlarged. As stated above, this phenomenon is more common in *japonicum* than in *mansoni* infections. This phase of the disease bears a striking likeness to Banti's syndrome and has often been confused with it.



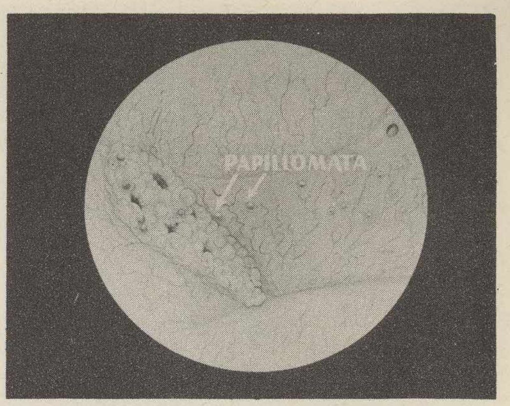
Rectal papillomata are common in *japonicum* and *mansoni* infections, because of passage of the eggs.

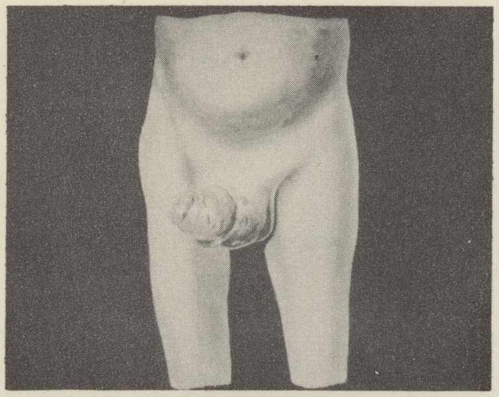
Continuing infection, and the constant repetition of the process of abscess formation, healing, and scarring does irreparable damage to the intestinal wall. The wall is thickened and there is extreme papillary proliferation of the mucosal epithelium, with the formation of adenomatous polyps. Intestinal carcinoma often accompanies schistosomiasis.

The obstruction of the hemorrhoidal vessels by the worms and eggs may lead to polyps and extreme proliferation of the anus and rectal mucosa. These manifestations are seen only in a fraction of long-standing cases in hyperendemic areas.



In schistosomiasis hematobium any pelvic structure may be involved. In the heavily endemic areas pyelonephritis and hydronephrosis are frequent complications. Chronic cystitis may result in papilloma formation. Ureteritis and urethritis are common, and urinary fistulae may occur.

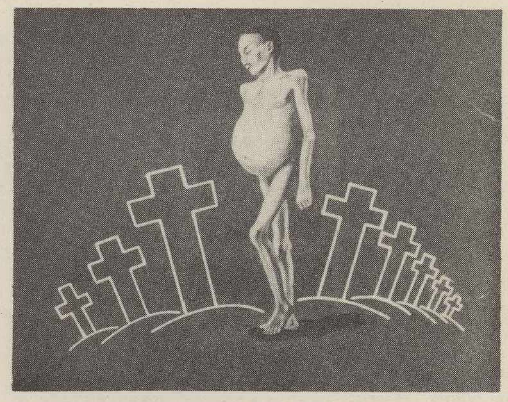


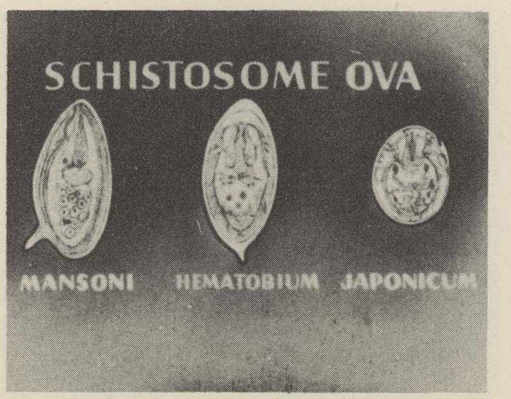


Elephantoid external genitalia occur and there may be multiple sinuses leading to the perineum, scrotum, and rectum. The association of bladder carcinoma and *S. hematobium* is common. Again it should be emphasized that only extreme cases may show these pathologies.

All moderate and heavy schistosome infections of long standing eventually show anemia and cachexia.

Intercurrent infection is common in all stages of the disease. Abscess formation commonly leads to infection by other organisms. Quite often this contributes to the general debilitating character of this disease and might be listed as a secondary cause of death. Tissue damage in unarrested and progressive cases is severe, and in all moderately heavy infections would be enough alone to be the cause of death. Severe damage to the genito-urinary and gastro-intestinal systems, as well as liver failure from extreme cirrhosis, might be listed as the primary causes of death. The presence of a severe anemia is probably not due to any great loss of blood, but to the interruption of hemopoietic processes by the general systemic allergic and toxic manifestations of the parasite and its products.





All the major pathology resulting from schistosome infection is caused by the eggs, which are easily recognized and are diagnostic of the species.

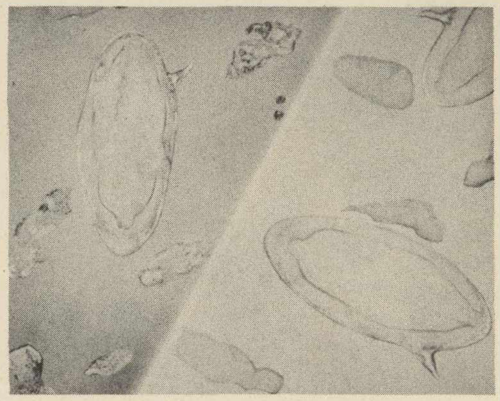
S. hematobium eggs are oval in shape, have a yellowish-brown transparent shell and possess a distinct *terminal* spine. They measure 112 to 170 microns long by 40 to 70 microns wide.

S. mansoni eggs are oval in shape and possess a yellowish-brown transparent shell and have a distinct *lateral* spine. They measure 114 to 175 microns in length by 45 to 68 microns in width.

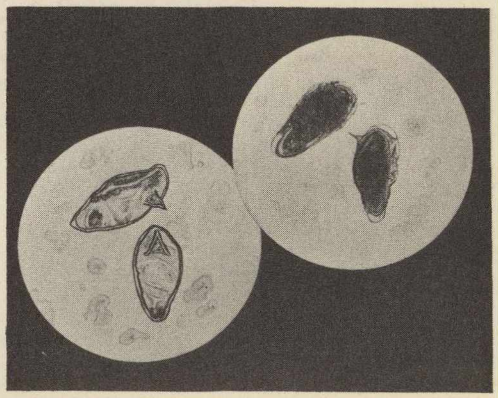
S. japonicum eggs are more roundly oval, and of a pale yellowish color. From a depression on the side near one end, extends a small spinose process, like a recurved hook, which is visible, if at all, only when the egg is properly orientated. These eggs measure 75 to 100 microns by 50 to 65 microns.

The eggs compose the major method of positive diagnosis of the three blood fluke infections. Normally the eggs of *S. mansoni* and *S. japonicum* are found in the feces, while those of *S. hematobium* appear in the urine, although the latter may also appear in the feces in some cases.

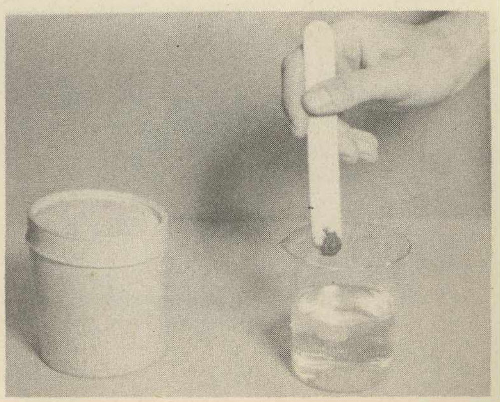
The easiest and perhaps best method of detecting the presence of eggs in feces is by use of the simple fecal smear. This method may not be satisfactory unless the eggs are abundant, but it is generally used as a method of initial examination. The technique of the fecal smear is extremely simple, but care should be exercised to select portions of the stool where the eggs are most likely to appear. These situations are on the outer surface of the stool in the small collections of bloody mucus which are often present. Since the eggs are extruded into the intestinal lumen from the mucosa, it follows that most of the eggs will be on the surface of the stool.



A small amount of the selected material is smeared with a disposable implement (an applicator or toothpick) in a small drop of normal saline or other suitable diluent on a glass slide. This preparation may be left unstained, or a drop of iodine added, and a coverslip placed over it. The eggs are large enough to be seen with ease using the low power of a compound microscope. Often the eggs are difficult to find in light infections and several preparations should be examined before turning to other methods of diagnosis. The eggs may be differientiated from those of other helminths by their characteristic size and shape and by the presence within the egg of a mature miracidium.



Schistosome eggs are usually not efficiently concentrated by the various flotation techniques which are so useful in other helminth diagnoses. The eggs are generally shrunken in saturated salt solutions and in the 33% zinc sulphate solution commonly used. The egg shells are apparently too fragile to withstand the increased osmotic pressure. In addition to the distortion which makes identification difficult, the ova may not float to the surface. However, Craig and Faust (1943) state that the ZnSO4 centrifugal flotation technique can be used efficiently for the concentration of *S. mansoni* eggs from feces, probably because the lateral hook still permits recognition even though the eggs are distorted.

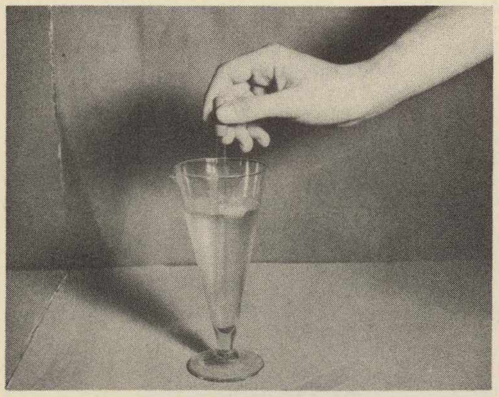


A fecal sedimentation technique is preferred, if fluke infection is suspected. A stool mass the size of a marble is stirred into two hundred fifty cc. of water.

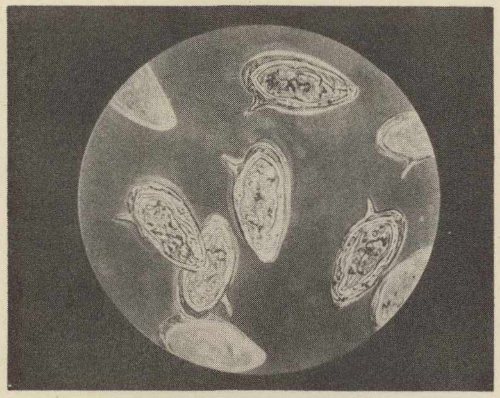
The suspension is sieved into a conical flask, thru coarse gause, cheesecloth, or a screen. An hour's settling permits pipetting a sediment sample, and examination by microscope of fecal sediment.

Various methods of fecal sedimentation are reliable for the concentration of schistosome eggs from the feces. Care should be taken to select the sample from likely areas in the stool. The sample should be thoroughly broken up and mixed with the water. In straining the suspension the use of a disposable material such as gauze or cheesecloth is desirable. If the same screen or cloth is used repeatedly, there is a chance of carrying eggs from one specimen to another. Several decantations and washings may be advisable for further concentration of the eggs, but sedimentation should be complete within 4 to 6 hours after dilution has been made, else hatching of the eggs may occur. The sedimentation may be speeded up by moderate centrifugation of the suspension for 30 to 60 seconds. The eggs are pipetted from the bottom of the container, in any case.

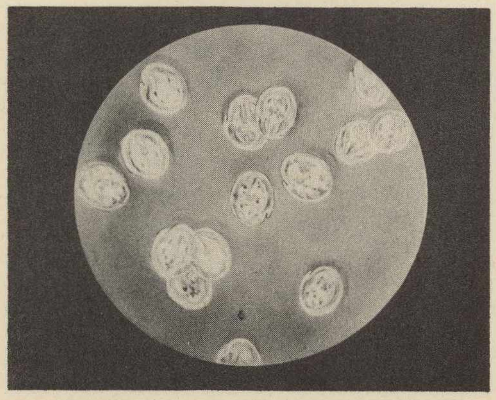
Another method of diagnosis takes advantage of the rapid hatching of the miracidia. The stool sample is diluted with clear non-chlorinated water, placed in a graduate or Erlenmeyer flask and allowed to stand for 12 to 24 hours. The miracidia collect in the top few centimeters of water and may be seen with a hand lens or pipetted to a slide and examined with a microscope. A more recent adaptation of this method utilizes the positive phototropic as well as the negative geotropic reactions of the miracidium. A distillation flask with a vertical side arm is used to contain the suspension. The fluid is brought up, after sedimentation, to the top of the side arm and the flask is darkened, leaving the arm exposed to light. After hatching, the miracidia will concentrate at the top of the side arm and may be pipetted off.



Another method of fecal diagnosis which is very useful is the acid-ether extraction method. The stool sample is placed in a small amount of 15% HCl, or 5% acetic acid, shaken vigorously and strained through cheesecloth. To the filtrate is added an equal amount of ether and the mixture shaken and centrifuged at 1500 R.P.M. for one minute. The contents of the tube are poured off rapidly, leaving only the sediment and a few drops of acid in the bottom. The tube is kept in a horizontal position to prevent the flow of debris down the side into the bottom sediment. This sediment is then transferred to slides and examined. This method is consistantly more reliable than other concentration techniques and reveals 10 to 20 times the number of eggs which may be counted in wet smears.

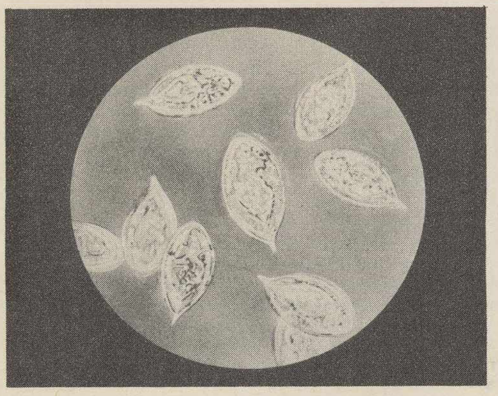


When discovered, *Schistosoma mansoni* eggs are large and almost invariably have a prominent lateral spine. The contained miracidium is generally conspicuously active, doubling and turning inside the shell. The eggs are sticky and almost always have many attached particles of fecal detritus to make the egg outline less clear.



It is rare to find a clear, lateral hooklet in either stained or unstained *Schistosoma japonicum* eggs. The eggs in this species are smaller and less conspicuous and the sticky shell with its accretions of detritus may be difficult to spot quickly in a microscopic field. The actively motile miracidium inside a living egg aids in the final identification.

The eggs of *S. hematobium* are characteristically found in the urine. They may be obtained by allowing the urine to stand and pipetting from the sediment after an hour or two, or the urine may be centrifuged moderately and the sediment examined. The eggs generally appear in the terminal urine, usually in the blood or pus discharged at the end of micturition, so it is this portion which should be examined. Occasionally the eggs of *S. hematobium* are found in the feces and in suspected cases fecal examination should be conducted. The eggs of this species have prominent terminal spines.



Although detection of the eggs is the most reliable positive diagnostic method for the schistosomes, other methods have been investigated and may be useful. Clinical diagnosis is extremely valuable in detecting early cases. A history of cutaneous lesions after exposure in endemic centers, urticaria, eosinophilia, and pulmonary disorders are all symptoms of early infection. The later pathologies are more striking, but all manifestations must be differentiated from those associated with such diseases as typhoid fever, nephritis, tuberculosis, dysenteries, hepatic cirrhosis, malignancies, and splenomegalies.

Schistosomiasis produces an increase in euglobulin and, provided leishmaniasis and other infections can be excluded, Napier's aldehyde test or similar tests may be used for confirmatory diagnosis.

Serological and intracutaneous tests may be of value in asymptomatic cases, in old infections where egg extrusion is prevented by fibrotic changes, and in early infections before eggs are produced. Alexin-fixative, precipitin, and intra-cuteneous tests show a group reaction for schistosomiasis with antigens prepared from adult worms or cercariae. Precipitin reactions are positive in 70% to 80% of infected individuals, but there is also a small percentage of positives in uninfected persons, mostly syphilitics. The intra-cutaneous test, using cercarial or adult antigens may be very useful in detecting infections. Only about one percent of infected persons fail to give positive reactions, but only about 60% of the persons giving a positive reaction show eggs in the feces. The positive reaction persists for a considerable length of time following elimination of the disease.

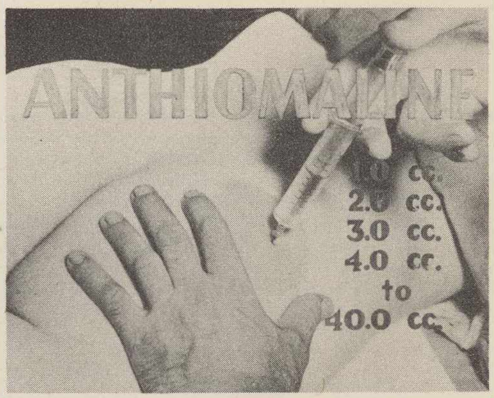
Once diagnosis is made, treatment must begin at once, to interrupt the progression of tissue damage. Four drugs are at hand: tartar emetic, fuadin, emetine, and anthiomaline.

Tartar emetic was the first anti-schistosomal drug used with success and was introduced in 1918. According to Stitt this drug is given intravenously on alternate days over a period of 4 to 6 weeks. The initial dose is usually ¼ to ½ grain dissolved in 20 minims of distilled water and diluted with an equal amount of normal saline, and it is increased by ½ grain until a dose of 2½ grains has been reached.

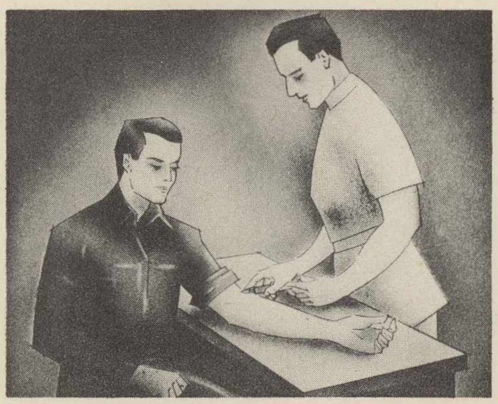
A total dose of 25 to 30 grains is usually sufficient, but it may be necessary to repeat the treatments if the first course is not successful. Treatment must be cautious since some persons are markedly intolerant of the drug. The drug is a depressant and the patient should remain in a recumbant position for at least an hour after each administration. Toxic doses may cause fatty degeneration of the liver, kidneys and heart, with congestion of the dura mater and cerebral vessels. In patients with concurrent cardiac, pulmonary, or hepatic disorders the drug is usually contraindicated.

Fuadin, or neoantimosan, is a trivalent antimony compound (antimony-pyrocatechol-disulphonate of sodium) and was introduced in Egypt in 1929 for the treatment of schistosomiasis. It can be given intramuscularly on alternate days without much danger of local irritation or sloughing at the site of injection. The course of treatment consists of 1.5 cc of a 7% solution on the first day, 3.5 cc of the same on the second day, and 5 cc on alternate days from the third to the seventeenth day. Cure may be effected in 19 days, and it has been reported to be 97.6% effective. The treatment usually causes no nausea, vomiting, coughing, or rigors and is considered to be much less toxic than tartar emetic. Contra-indications, however, are probably similar.

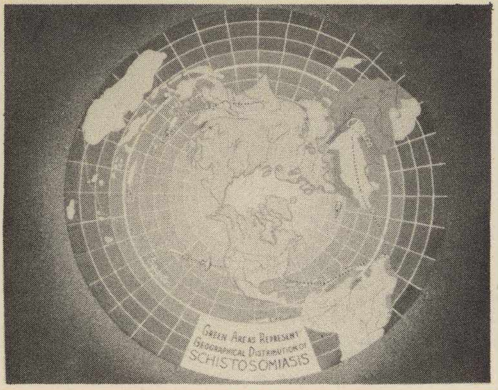
Anthiomaline (antimony thiomalate of lithium) is the newest anti-schistosomal drug, having been first tried in 1935. The drug is more toxic than fuadin but less so than tartar emetic. The toxic symptoms consist of thirst, nausea, vomiting, headache, lassitude, and articular pains. The amount of treatment necessary for eradication of the infection varies from 21.5 cc to 55.5 cc of a 6% solution. The maximum single dose, 4.25 cc, is given on alternate days up to 14 doses. Six to nine intra-muscular injections will cure the majority of cases. Contra-indications are the same as for tartar emetic.



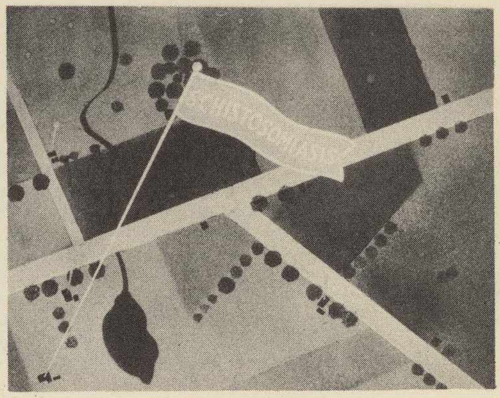
Intravenous antimony compounds are definitely contra-indicated in patients with advanced hepatic cirrhosis as well as those with anemia, heart disease or nephritis. It must be remembered that individual intolerance to all these compounds is common and that the patient should be under strict observation throughout the course of treatment, especially for a period immediately following the administration of the drug. The occurrence of intercurrent infections may also contra-indicate treatment.



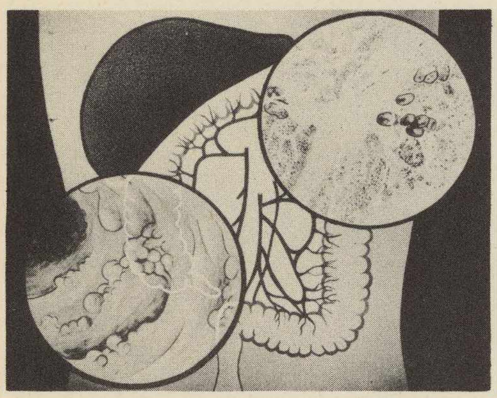
Prompt treatment of an early diagnosed case is important. Treatment cannot repair damaged tissue — it can only prevent further damage. Also, in early infections, the patient has not as yet become debilitated and is able to withstand the treatment with fewer adverse effects.



The possibility of the spread of schistosomiasis in this country has not as yet been thoroughly explored. It is known that at least one potential snail host *(Tropicorbis havanensis)* is already present in the country (Cram et al, 1945), and the snail fauna has not yet been thoroughly investigated. There are situations in the United States where conditions are such that, given the snail host and a reservoir of infection, the disease could thrive. With the return of our armed forces from endemic centers all over the world, and with the onset of the expanded world travel expected in the postwar period, there is a good possibility that reservoirs of infection will be established. Diagnosis of these reservoirs must be made speedily so that treatment may be initiated.

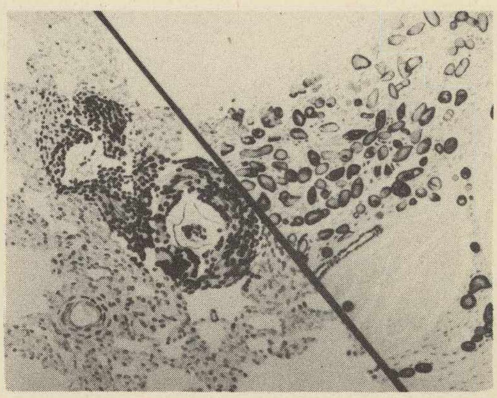


Confirmed cases must be reported to the health authorities promptly so that they may take steps to prevent the establishment of the disease. It is necessary for the carrier of the disease to be educated as to his personal responsibility in preventing its spread; it must be ascertained if the patient lives in a situation or a type of environment which might lead to spread of the disease; and his locality must be investigated in an attempt to discover the presence of potential snail intermediate hosts.

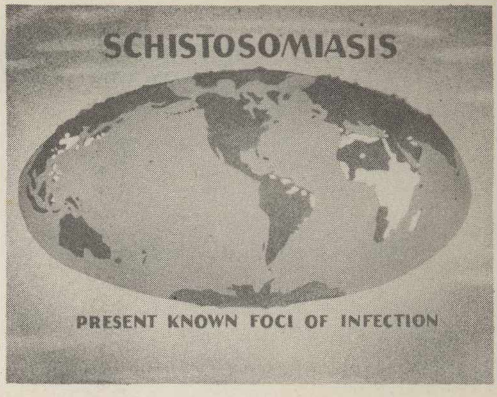


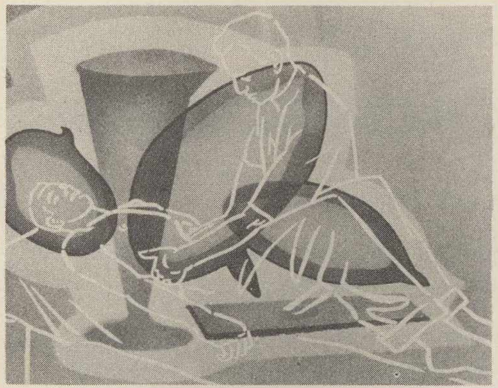
Continuing infection with *S. mansoni* and *S. japonicum* may be responsible for intense and irreversible damage to the liver, spleen and intestinal tract. In the heavily endemic areas more extreme pathological changes are the result of continuous infection and reinfection. Infiltration and encapsulation of eggs in the liver produces progressive cirrhosis of that organ. Splenomegaly and anemia are common. In the intestine papilloma formation, fistula development, extreme fibromatous proliferation, and carcinoma are commonly associated with the long-standing disease. Morbidity is high and mortality is not uncommon in the endemic areas.

Uninterrupted infection with *S. hematobium* may lead to extreme pathology. The most obvious changes are in the organs and tissues of the pelvic region, especially the bladder wall, where the formation of abscesses and pseudo-tubercles may be followed by extensive fibrosis. In areas where reinfection is common, more extreme pathologies are seen. Papilloma and polyp formation is common, and carcinoma of the bladder is frequently associated with the infection. All types of genito-urinary disturbences are common sequelae, and the lesion in the male may extend into the penis with fibrosis of the sheath and elephantiasis of the organ from blockage of the scrotal lymphatics. Often there are multiple sinuses leading to the rectum, scrotum and perineum, and intercurrent infection is almost invariably present.



Although it may be hoped that this disease will be stamped out throughout the world, this possibility is fairly remote at the present. However, it is possible to prevent its spread to this country. Every possible energy is being exerted to investigate the probability of its establishment. The presence of the snail host is being investigated. An effort is being made to discover cases in the armed forces which are returning from the endemic foci and these cases are being treated. However, cases often do not appear for a considerable length of time after they are contracted and cannot be discovered until they return to civilian life and their homes.





It must be emphasized that, in order to prevent irreversible damage to infected persons and to aid in preventing establishment of schistosomiasis in this country, cases must be diagnosed correctly and early and treatment initiated immediately.

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