# Schistosomum Mansoni and Schistosomatosis observed in Brazil

by

**ADOLPHO LUTZ, M. D.**

(With Plates 37–43).

Biology and evolution of the trematodes belonging to the genus *Schistosomum* were but little known until a few years ago, but since 1911 several papers were published which gave the solution of the most important problems for four species. I report here the results of my investigations, directed mainly to repeating and controlling the recent experiments in connection with the only species known in Brazil, yet also to determining the local species of the intermediary host and the conditions of infection in this country. In order to give more pratical value to my paper and to help the orientation of the readers, I decided to recall briefly the most important facts in connection with the parasitism of all the schistosoms and particularly the species *Mansoni*. Of litterary references I only give the most important and those in closer connection with my paper; for the rest I may refer the readers to the list given by LEIPER (1915) which is easily obtained and very extensive, containing 529 numbers.

I shall first consider the historical and and geographical part of our knowledge concerning the genus *Schistosomum* and the diseases caused by the same.

## Schistosomatosis or Bilharziosis in Africa.

The troubles caused by the African species of *Schistosomum* were known long before their cause and existed in remote periods, as the examination of mummies has proved. Since the invasion of Napoleon until our time they were very common there. In this classical field of observation the parasites were discovered in 1851 by BILHARZ who called them *Distoma haematobium*, on account of their inhabiting the blood vessels. He was well fit for such studies and recognized that this very peculiar trematode was specially caracterized by separate and bimorphic sexes, a quite new and unexpected fact. The name *Schistosoma* WEINLAND, now generally latizined *(Schistosomum)*, seems to apply to the male whose body has a fissure, opening a longitudinal furrow in which the female is carried. Hence the name *Gynaecophorus*, given by DIESING in 1859. In the same year COBBOLD introduced, in honour of the discoverer, the name *Bilharzia* which, as well as the derived expressions *Bilharziasis* and *Bilharziosis*, was commonly employed.

(BLANCHARD stated that WEINLAND'S name was published on August 5th 1858; the one of DIESING, proposed in a session of the Academy of Science in Vienna, was published Oct. 21t and COBBOLD'S name Jan. 20th, 1859; therefore he concluded that WEINLAND'S name ought to be accepted. (LAVERAN & BLANCHARD. Les Hématozoaires II, p. 40). This name, formely little known, is generally used in the later litterature).

Already the first observations in Egypt showed that the lesions might be localized in the urinary system or in the intestine or in both, while the eggs found in them had either a terminal or a lateral spine. As both processes were very common, they were often combined in one patient who then furnished both species of eggs. Therefore the general opinion went on attributing both processes to the same parasite (although the idea of a double origin was very soon suggested). This was due mainly to some observations, always brought forward in the discussions and apparently convincing. Today, however, it is evident that, either in the observation or in the interpretation, there occurred some error, not at all unlikely to happen. This unfortunate accident proved an enormous drawback for the right understanding, of these infections.

The first observation of a focus where only eggs with terminal spines ocurred, was made by HARLEY in the South of Africa. He thought the parasite was altogether different and gave it the name: *Distoma capense* (which, in my opinion, ought to be still used for that form). In 1912 BOUR found in Mauritius 34 boys voiding Sch. eggs with their urine. He did not mention the position of the spine, nor eggs in the stools. Many observers found both forms of eggs in Tunis. In the Soudan. in the lake territory and generally in hot regions with plenty of, more or less, stagnant water, the disease of the urinary system is common. It is also found in the islands of Madagascar, Nossi-Bé and Réunion. The intestinal form is often found together with the other and aparently alone in the Belgian Congo.

**Schistosomatosis in other continents.**

*Schistosomatosis* localised in the urinary system has been found in many endemic foci of Asia. As for America, it is quite certain that there never has been an endemic focus of this form; a few cases reported were apparently only seen in people, who had arrived or returned with an infection contracted in other continents.

It is remarkable that in tropical America which imported so many slaves, the disease of the bladder never took root, while it becomes every day more evident that the intestinal form is widely spread in the West Indian Islands and on the South American continent. It is certain that both forms have been imported over and over again but only one spread. This is now easily understood, as we know that the possibility oi localisation depends of the kinds of fresh-water shells found in the place.

**Schistosomum haematobium BILHARZ includes two species.**

The idea that two different species were united under the name *Sch. haematobium* was again sustained in 1893 on the base of observations made in America. The fact that in 1876 SONSINO had found a second species *(Sch. crassum)* in cattle and still more the discovery of the *Sch. japonicnm* in 1903 helped to sustain this supposition. Iu 1907 SAMBON introduced the name *Sch. Mansoni* for the American species; it was generally accepted, though this form ought to have kept the name *haematobium*, the other having been distinguished nnder the name *capense* HARLEY.

The double value of the species was denied by several authors and principally by LOOSS who tried to explain the differences of the eggs by quite unconvincing arguments. It is strange that this author, who so violently sustained the unity, should at other times have separated new species and even genera with no better arguments, However, nowadays this discussion has lost all importance, as the double nature of the ancient *Sch. haematobium* is generally recognized.

There are now six more species known, all of which have different eggs, of one form only).

Some authors claim to have found eggs of both forms in the intestine and in the urinary organs. Excluding evident mistakes, these observations are altogether rare and mostly old; they refer to double infections of long standing and several explanations have been given for the abnormal localisation in these cases. In America a great number of observers failed to find a single egg with terminal spine amongst thousands with lateral ones; it must however be remembered that a lateral spine in certain positions may appear terminal, unless the egg be rolled. As seen in figs. 10 and 11, they may have an obtuse prolongation situated at the more distant pole and very different from a spine. The localisation in the urinary systeme causes different and very striking symptoms, while those of the intestinal form may easily pass unnoted. Already WUCHERER searched for Schistosomum eggs in cases of haematuria, observed in Bahia, and failed to find them, though in the same place the other form occurs frequently. In a great number of urine examinations which I made during the space of 38 years, I failed to find a single egg of *Schistosomum* though their form was well-known to me, a fact which, combined with the experience of many of my colleagues, is sufficient to exclude the existence of this fluke in the more known parts of Brazil. On the other hand I examined the stools of about twenty patients of *schistosomatosis* of the intestine, acquired in the north, in some cases very often, without finding one egg with terminal spike. My observations are confirmed by those of Dr. OSWINO ALVARES PENNA, who also observed some of these cases and many others, and agree with the results obtained in the West Indian Islands, in Dutch Guiana and in Venezuela.

In another place, I shall explain the characteristics which distinguish the two species. This paper is limited to *Sch. Mansoni* SAMBON, which is the only one found in Brazil, and, indeed, in the whole of America, with the exception of imported cases. In the latter sometimes *Schistosomum* has been found located in the urinary system; this generally happens in those of African origin. With the increasing emigration of Asiatics, there may appear cases of Asiatic origin, due to *Sch. haematobium* or even *japonicum*. The transmitter is different from all our indigenous mollusks, so that the importation of the Japonese parasite need not be feared.

**O Schistosomum Mansoni na America.**

Since the year 1902, cases of *Sch. Mansoni* have been observed in America or in persons there infected. The first centres observed or pointed out by the patients were in the West Indian Islands. Here we may quote the cases of MANSON (1903, infection in Antigua or in one of the other West Indian Islands), of LETULLE (1903 in case of Martinique), MACDONNELL (1905, case of Culebra), LAHILLE (1906, ibid.). In Porto Rico which is an important centre, GONZALEZ-MARTINEZ observed and published the first cases in 1904. Later on, ASHFORD, KING and GUTIERREZ IGARAVIDEZ often found eggs, while they were studying endemic ankylostomiasis. The studies of these authors, as well as later work, prove that Martinique, Guadeloupe, Vicques, Culebra, Portorico and Cuba must be counted amongst the principal centres (v. HOLCOMB, 1907).

In medical literature, we find unexplained cases of urinary schistosomatosis with the eggs belonging to it, observed by CORTEZ in 1905 in a native of Guatan, Guatemala. Dr. BUTLER is also quoted as having observed a patient from Porto Rico in San Juan, who evacuated two eggs with terminal spine in his urine, without knowing where he contracted the disease. As a great number of patients have been examined in Porto Rico by competent physicians there is little probability of that place being an endemic centre of this form of Schistosomatosis; the doctors of this island are unanimous in recognising the frequence of *Sch. Mansoni*, and the lack of eggs with terminal spine.

Other cases, observed in the zone of the Panama Canal by ZEILER (1900), appear in the literature without information as to the zone of infection. Amongst these one case is mentioned where the two forms of eggs coexisted with the two forms of infection. If the case be authentic, I an inclined to consider it as an infection, imported from another continent.

In the South-American continent, cases were reported from Dutch Guiana (FLU 1908), Venezuela (BREM, JESUS RISQUEZ), Columbia (BATES) and Peru. According to a recent publication by JESUS RISQUEZ, it seems that the infection is very common in Venezuela, as he found it in 25 % of the autopsies made in Caracas, which means an intense focus. He also studied the pathological anatomy.

In 1905 BLUMGART of New York observed *Sch. Mansoni* in a German, probably infected in Brazil, as he had lived in that country for 7 years.

In 1908 and 1909 Dr. M. PIRAJÁ DA SILVA made a series of communications by which he proved the frequency of intestinal Schistosomatosis in Bahia. He tried to characterize the parasite as a different species which he called *Sch. americanum*. He also described a cercaria found in Bahia under the name of *Cercaria Blanchardi*. Subsequent studies showed that as well its general form, as its host. a large *Planorbis*, agree with the supposition that he was dealing with the cercaria of *Sch. M.* JOHN MILLER and several other writers also recorded observations from Bahia.

As for Rio de Janeiro Sch. eggs-with lateral spines were found in stools by FARIA, in tumours of the rectum by VIANNA and in the pancreas by D'UTRA. Though these and other observations were made here, the anamnesis, when known, pointed to an infection in the states of the North of Brazil. The same may be said of many cases observed by PENNA and others where the eggs were discovered while looking for Necator eggs. The cases ocurred mostly in sailors and marines who were infected before entering the schools, mostly be bathing in ponds containing fresh water shells. Some of the infections had taken place many years ago. The patients hailed from the states Bahia, Sergipe, Alagoas, Pernambuco, Parahyba and Rio Grande do Norte which are undoubtedly infected zones. To these we may add Goyaz where NEIVA, on one ocasion, observed characteristic eggs. Infection probably also existed in a place in Ceará, in a swamp near Obidos and in a "lagoa" in Espirito Santo. The infection is so little characteristic, as to be recognised only when either a microscopical examination of the stools or a careful post mortem examination is performed.

It is only due to the stool examinations, now commonly made for the research of *Necator* and *Uncinaria*, that the infection was discovered in so many new centres. The indispensable conditions for the existence of endemic centres are, on one side, a hot climate, on the other, the presence of a species of Planorbis which is apt to become an intermediate host. In Brazil *Pl. olivaceus* and at least two more species are easily infected, but they do not seem to exist in Rio de Janeiro or to the south of the city.

In 1916 the institute sent one of its servants, named THEOPHILO MARTINS, to Aracajú. He verified the infection in several persons who used to bathe in ponds where *Planorbis olivaceus* was common. Of these he brought a great lot which I used for infection. We also received specimens from our colleagues Drs. PIRAJÁ and OCTAVIO TORRES and used them for experimental infection. In the last lot I found some naturally infected specimens which furnished living cercariae,

**Recent observations made in the North of Brazil.**

A special commission was sent by this institute in the second semester of 1917, in melho, como dieta principal. No fim de um certo numero de dias (de noventa a cento e tantos) apareceram casos tipicos de beriberi nos do grupo "A" emquanto os do grupo "B" nada sofriam. Si no grupo "A" era mudada a dieta os doentes curavam-se e o beriberi dasaparecia. Individuos do grupo "B" foram transferidos para o local do grupo "A" vivendo de mistura com os individuos atacados. Si comiam arroz vermelho não adquiriam beriberi; si comiam arroz polido eram no fim de certo tempo, atacados da molestia.

Ficava de uma vez provada a não contajiosidade da doença e a sua origem alimentar. As condições da experiencia, para evitar um erro de observação foram as mais rigorosas possiveis. Todas as precauções foram tomadas para tornal-as rigorosamente exatas e verdadeiras as concluzões. Na mesma ocasião esses ilustres pesquizadores reproduziram as experiencias em animaes, chegando á concluzão da identidade etiolojica e mesmo sintomatica das duas molestias.

FLETCHER, em 1909, tratou 123 habitantes do Kuala Limpur Lunatic Asylum com arroz polido e 123 com arroz não polido, no 1º grupo observou 43 cazos de beriberi: no 2º grupo nenhum. Os 2 grupos trocaram de edificio porém nenhum cazo ocorreu nos alimentados com o arroz vermelho. Então trocaram de arroz. O 1º grupo passou a usar o arroz vermelho, e o 2º o arroz polido, nenhum cazo mais ocorreu no 1º grupo mas logo o beriberi se desenvolveu entre as pessoas do 2º grupo que estavam, então, usando o arroz polido.

No Boletim de Saude nº 12, publicado pelo Departamento do Interior do governo americano das Philipinas, verifica-se que nos scouts dos Estados Unidos os mesmos resultados foram obtidos. Entre estes soldados a molestia se tinha espalhado muito. Em um ano foram registrados 600 casos. Depois do uzo do arroz vermelho começou a molestia a desaparecer e não foram mais registrados outros casos entre as tropas. O governador geral lançou uma ordem proibindo o consumo do arroz polido nas instituições do governo.

E por toda a parte, diz o relatorio, a molestia desapareceu. Alem disso ficou provado evidentemente que os poucos casos observados eram devidos ao fato de alguma instituição não ter obedecido extritamente o regulamento, no que diz respeito ao uso do arroz polido. Nesse boletim o governo pedia a todas as pessoas abastadas que usassem o arroz não polido, como um exemplo aos ignorantes e aos não favorecidos da fortuna. A repartição de higiene propõe uma taxa de 4 centavos por kilo de arroz polido para tornal-o um alimento dos ricos, a quem não pode fazer mal, pela existencia de outros alimentos na sua meza.

Em 1913 publicavam em lingua castelhana R. S. STRONG e B. C. CROWELL os resultados das suas investigações (de 1912) e tal é o rigor scientifico desse trabalho que o considero o argumento maximo, o argumento definitivo em relação a etiolojia alimentar do beriberi. O valor principal destes estudos consiste no fato de ter sido o metodo experimental aplicado ao proprio homem, encarando o problema por todas as suas faces, completando, assim, as experiencias de FRAZER, de STANTON e de FLETCHER. Convencidos de que MANSON, SCHEUBE, LE DANTEC, MARCHOUX, WRIGHT, CASTELLANI, SHIBAYAMA não apresentavam provas suficientes em defeza da teoria infecciosa procuraram STRONG e CROWELL reproduzir a molestia excluindo a influencia de microorganismos especificos. STRONG e CROWELL reconhecem a importancia do estudo da polinevrite galinarum, pois que as experiencias sobre as aves foram proveitosissimas e elucidaram muitos problemas relacionados com a etiologia e a cura do beriberi; mas que, sem experiencias, identicas, diretamente feitas no homem, nada de absoluto e com criterio scientifico se poderia afirmar. Estas experiencias memoraveis foram executadas na prisão de Bilibid, em Manilla, prisão cujas condições hijienicas *são quazi ideaes*. Com a sanção do governo, um certo

1916 ITURBE and GONÇALEZ report that the host of *Sch. M.* in Venezuela is *Planorbis guadelopensis.*

1917 It is shown that some of the brazilian foci depend on *Pl. centimetralis* and that *Pl. guadeloupensis* also occurs.

1918 The host of *Sch. Spindale* is discovered by GLEN-LISTON and SOPARKAR.

## Descriptive Part.

### The genus Schistosomum.

(Figs. 1–8),

The genus *Schistosomum* comprises different species of blood flukes which posses an oral and an abdominal sucker and were therefore at first included in the genus *Distoma*, now usually latinized *Distomum.* This genus is now subdivided in many others forming the family *Distomidae. Sch.* is distinguished from most of them by having the two sexes distributed on two individuals instead of having them united in one. Another characteristic is the *habitat* in the blood vessels to which these flukes are well adapted.

Similar characters are found in a few more genera, allied and only recently separated. They form a sub-family which may be called *Schistosominae.* I quote the genera *Bilharziella* and *Ornithobilharzia,* observed in birds 4).

Sexual dimorphism is very marked in *Schistosomum.* The male has a flattened and rather wide body, well developped muscles and pointed skin scales which assist it in holding its place ayainst the blood stream; the female has a filiform body like a nematode; her muscles are weak and the scales are either absent or very small,

After the cephalic part the body of the male widens out, though the lateral parts are not flat but inwards curled, thus constituting the *canalis gynaecophorus* which generally contains one, rarely two or more females. The genital system is reduced to a subdivided *testis* (sometimes followed by a *vesicula spermatica)* and an excretory duct; there is no *cirrhus.*

The female has a *corpus vitelligenum,* an ovary and a long tube corresponding to *uterus* and *vagina.* A small segment which contains the first (and sometimes only) completely formed egg, may be called *ootype.*

In both sexes no pharyngeal or oesophageal bulb exists and the intestine is first double and afterwards simple, in varying extent.

(There are three species living in man and five more found in domestic animals, all of them easily distinguished by their eggs. The human parasites also occur in apes and rodents (spontaneous or experimental infection), while *Sch. japonicum* is also found in most of the domestic animals).

### Description and differential caracters of Schistosomum Mansoni.

(Fig. 1–8, 15.)

The anatomy and morphology of *Sch. M.* were studied by the discoverer and also by LEUCKART, R. BLANCHARD, CHATIN and FRITSCH before 1888; the results were discussed by R. BLANCHARD in 1889 and by LEUCKART in the second part of his classical treatise, in collaboration with LOOSS. The problem might have been practically exhausted, if the authors had worked on one species only, (and not with a mixture of two) or only on the form found in the urinary system. For this reason the descriptions have only a relative value and ought be corrected for each of thetwo species, confounded under the name *Sch. haematobium.*

The differences were already indicated by PIRAJÁ, FLU, HOLBORN and other authors who studied the american species, but, as they had no occasion to compare fresh specimens of the other species, the value of some differential caracters might have remained somewhat doubtful; but LEIPER who ultimately had occasion to compare both species in Egypt, quite confirmed the correctness of the most important characters which make the distinction safe and easy. I also found in our specimens all the caracters which he attributes to the intestinal form of Egvpt; this is undoubtedly identical with *Sch. Mansoni*. As shown by a recent communication, GONZALEZ MARTINEZ also came to this conclusion.

The genus characters common to both species are the following:

Localisation in the blood vessels and alimentation by blood. Existence of two sexes; males with *canalis gynaecophorus*, nematoid females. Eggs without lid, containing a miracidium when voided. Penetration of the miracidium in a freshwater mollusk followed by formation of sporocysts and cercariae which emigrate spontaneously. Cercariae without pharyngeal bulb, with bifid tail and large glandular cells, infecting the ultimate host by boring through the skin.

For distinguishing the two species the following apparently well established differences are sufficient:

**Haematobium.**

♂ *Testis* showing 4–5 lobes.
Anterior *Vesicula seminalis*.
♀ *Ovary* in the anterior half of the body.
Ripe egg with terminal spine.
*Uterus* long, with many eggs.
*Corpus vitelligenum* short in the caudal forth.
*Coecum* short.
First stages in *Physopsis*.

**Mansoni.**

*Testis* with about 8 lobules.
No *vesicula seminalis* to be seen.
*Ovary* in the posterior half of the body.
Ripe egg with lateral spine.
*Uterus* short, with one egg as a rule.
Dto. long. extending over the last two thirds of body.
*Coecum* long.
First stages in species of *Planorbis*.

Beside these, other differences have been indicated which refer to the dimensions of the body and the suckers, the distance between the ends of the coecum and the body and the armature of the skin in the two sexes, but I consider them less certain and evident. The form of the testicle and the intestine may vary a little, but not to a degree affecting the distinction of the species.

For the clinical diagnosis the form of the egg, found in the stool, and the localisation of the symptoms are sufficient.

In dead specimens the dimensions depend not only on the method of fixation, but also on anterior conditions which determine the contraction or relaxation of the muscles. The latter influe so much on the live specimens, that any given dimensions have only a relative value. Ancient authors did not distinguish and the newer observers failed to compare the two species under identical conditions. Of modern authors BRUMPT gives the following dimensions for *Sch. haematobium:* Male, length 10-15 mm., width not more than 1, female 15-20: 0,1-0,2 mm.; Pirajá for *Sch. M.*: male 12: 0,558 in the middle, female 14,5-15: 0,168 mm.. My impression is that *Mansoni* is altogether somewhat smaller than *haematobium*.

The colour varies according to circumstances and is not likely to be constantly different in the two species.

**The Eggs of Schistosomum Mansoni. Characteristics of the eggs found in the stools.**

The evolution of *Sch. Mansoni*, outside of the human body, begins with the eggs voided in the stools. These deserve special study as they furnish the principal means of diagnosis. It is impossible to arrive at a sure diagnosis by any other means and indeed the frequent occurrence of the parasite in South America was discovered only by constantly searching for the eggs of intestinal parasites.

The *Schistosomum*–eggs are rather large but the shell is transparent and delicate. They are, therefore, not well seen in opaque preparations and may be easily squashed. Due to the scant production they are rare and easily escape observation, when the females are not numerous. Slight or recent infections cannot be safely excluded, as the eggs take some time to reach the intestine, when they are not altogether retained, which seems to happen frequently.

Examination is rendered easier by washing the feces, followed by sedimentation or centrifugation. With these may be combined the use of wire netting or muslin which retain the larger bodies. Thus we obtain a sediment that contains almost exclusively globules of starch and eggs of parasites which easily found.

The appearance of the egg is well perceived in our illustrations. The normal eggs (Fig. 15). are furnished with a lateral spine only and contain a perfectly visible embryo. In pathological eggs the size may be diminished while no embryo is found. One of the poles may show a protrusion, more or less considerable (Figs. 10 and 11), but this could only be taken for a terminal spine when the examination is carelessly made. As yet there has been no mention of two lateral spines. Figure 12 shows the only case of this rare anomaly which I found while examining thousands of eggs. The eggs, with or without embryo, may be calcified or encrusted with crystals. (Figs. 9,13 & 14). Recent descriptions of eggs with lateral spines have been published by HOLCOMBE and GONÇALEZ-MARTINEZ. Both have illustrations which are rather schematic, especially those of the latter. I also show a drawing from nature. The outside shell of the egg or chorion has a regular oval form, interrupted only by the apex of the spine, which is sharp and compact, whilst the base is conical and hollow.

The dimensions of the eggs are rather variable in the normal state. HOLCOMB. gives 112 to 162 for the larger axis and 60-70 for the lesser. Taken from thirty measures, GONÇALEZ-MARTINEZ indicates a medium of 147f or 67, 69. These dimensions agree better then those of the spike, of which the length, according to the first author, is 15-17, against 22,7 of the latter, and the width 7,5, but this may be due to the way of measuring. The point of insertion, according to HOLCOMBE, is distant from the nearest pole for the fourth part of the longitudinal axis.

The interior membrane (amnion or vitellary membrane) is near the other, but does not enter the spine and leaves an enlargement of varying thickness at the poles; as a rule, it is generally larger at the pole farther from the spine, which many be considered the anterior, as it is generally occupied by the cephalic extremity of the embryo. Thus the spine points backwards.

Both membranes are fine and transparent, but while the chorion is more yellowish, the amnion is hyaline; this pigment however, as in other eggs of entozoa, is derived from the fecal medium, and is absent in the eggs protected by a thick covering of mucus.

## The embryo or miracidium inside the ripe egg.

The normal eggs are voided with the embryo alive and completely formed. The transparent membranes do not prevent examination, but weak powers do not allow of the distinguishing of all structural details. Using immersion lenses, the cover glass must be fixed on the slide, which may be done with paraffine or turpentine. Thus we may obtain clear images, but the outlines of the internal organs are very delicate and their superposition prevents their being seen all in one egg. The embryo is covered with cilia which in the anterior part are longer and point forwards. The bucal papilla is bare and on the rest of the body the cilia are turned backwards.

There are four tubular openings, of the excretory system showtng vibrating membranes, perceived in some extension.

The existence of contractile fibres, running in two or three different directions, is indicated by the lively movements the embryo makes before bursting its shell. They are not, however, so easily seen and demonstrated, as might be concluded from the perusal of the litterature.

There is also a bagshaped gastro-intestinal organ, easily perceived when full of yolk granules. It communicates with the mouth by a wide tube which narrows towards the anterior end. The wall of this tube and of the sac are apparently flaccid.

On both sides of the stomach, a large glandular cell is easily seen, but I am not able to recognise in living specimens the nucleus, generally indicated in drawings. The excretory tube begins wide and narrows until it reaches the cephalic papilla where it bends outwards. When full, the glands and excretory ducts are very clear, the former may be turned inwards and cover the gastric sac. In fig. 15 glands and sac are not very full and show distinctly at the same level; the gland-cells are not granulated, as one might expect from some drawings of the embryo of *Sch. haematobium.*

I am unable to perceive clearly the nervous system, as it appears in some drawings. However, I see, under the organs just described and nearly in the centre, one large vesicular cell and a few smaller ones.

Their function seems like the one of a small balloon inside of a large one, giving to the body the rigidity and elasticity necessary for the movements. The rest of the body is formed by larger and smaller spherical masses; they are not very well defined and represent undoubtedly the germinal cells.

The outer and inner cilia only begin to move when the egg is in a liquid medium and the water penetrates by osmosis, as happens when the eggs are isolated by washing with fresh water.

## Ecdysis and free life of the embryo or miracidium.

(Fig. 15—17.)

The favourable conditions for the ecdysis consist in pure water, light and a temperature near to 30° C. In Rio de Janeiro there are many winter days which are not suited to its observation and in cooler climates the natural conditions with rare exceptions are unfavourable.

The best process for observing the free life of the *miracidium* consists in washing, straining and sedimenting stools comparatively rich in eggs. The sediment with little water is poured in small glass dishes and exposed to the sun. The same result mav be obtained by approaching an electric bulb, sufficiently to raise the water temperature to 30°. Even in the best of conditions, when the first miracidia appear soon, the ecdysis is never seen in all of them, probably because a certain number has not yet reached complete maturity. Keeping the rest in a cooler and less lighted place, the experiment, repeated once a day, still gives positive results in the next three or four days. Even after eight days, eggs with living embryo may be found but no ecdysis takes place.

Before the ecdysis we note the penetration of the water followed by a dilatation of the shell. The vitelline granules show lively molecular movement and all the cilia and vibrating membranes begin to play. Then we note from time to time an energetic contraction of the embryo which may turn completely inside the shell. The ecdysis is momentary and therefore easily missed. In one of my observations, it was proceded by very rapid and energetic rotation of the embryo which took a nearly globular shape.

The empty shell shows a spindle-shaped tear (which generally passes through its equator) and its aspect is quite as striking and characteristic, as that of the entire egg.

After leaving the egg, the *miracidium* stretches, taking a cylindrical form, and swims in large curves towards the light, until it is held back by the margin of the dish. With strong, oblique illumination it is easily recognized by its characteristic movement. (Confusion with certain infusoria and rotatoria must be avoided.) At a less favorable temperature the embryo becomes more pyriform and sinks to the bottom. The same happens, if several hours pass without its finding a suitable host.

Enclosed in capillary glass tubes and exposed in a refrigerator to very low temperatures, the miracidia become first pyriform, then immovable and finally die after a short lapse of time, unless they are soon removed. In the latter case they may reassume their áctivity. They are always more sensitive to cold than the *cercariae* and this explains the fact that an infection, already started in the antennae of a snail, may be interrupted in consequence of cold weather.

### Penetration of the Miracidia in Mollusks.

In order to watch the penetration I put a few snails in a deep PETRI's dish, adding water containing myracidia. A binocular microscope is very useful for this purpose but any lens with a weak power may be used. At first the miracidia continue their evolutions, sometimes passing close to the snails without taking any notice of them. Then they come nearer and nearer to the species they prefer. Suddenly, one or the other sticks on an exposed part. Others follow, but many remain refractory for a long time.

The species experimented upon belong to *Planorbis*, *Physa*, *Limnaeus*, *Ancylus* and *Ampullaria.* With rare exceptions (perhaps due to a previous contact with other species) the three last were completely left alone. The *Physa* and the redblooded *Planorbis* showed equal attractlon, the adults being prefered; contrary to my expections, the bigger they were the more attraction they seemed to offer. The point of predilection is the antenna which is very well suited for further observations. The rest of the head and the postantennial region are also frequently chosen. The well exposed pallium is little attacked in *Planorbis*, somewhat more in *Physa*; in both the foot is neglected.

As shown in the drawing the miracidium on penetrating has an elongate, almost cylindrical form. Its movements are similar to those of a rock-drill or the piston of a syringe. The time required for complete penetration is 10-15 minutes; afterwards the miracidium is seen extended in the subcutaneous layer, showing its cilia but with the glands empty. Sometimes after several attempts the miracidium drops again or leaves the point of attack without penetrating.

Up to date, only four species of *Planorbis* are known as intermediate hosts. They are *Pl. Boissyi* in Egypt, *guadaloupensis* in the Antilles, Venezuela and the North of Brazil, *olivaceus*, found in Bahia and Sergipe and used in most of my experiences, and finally *centimetralis mihi*, found in the northern states and also in Minas. The other species described in my monograph of the brazilian *Planorbis* are not suitable. In some, as also in *Physa*, the penetration is normally effected, but evolution is arrested after the first stages.

The miracidia, which try to penetrate in other regions than the antennae or near to the eye, fail to pierce the skin or die shortly afterwards; at least I never found the next stages in other points, though possibly a miracidium might pass through the respiratory opening and reach the visceral part.

My studies were all made on the antennae which are easily observed and may be removed without danger to the snail. Even the detached antennae of *Physa* and *Planorbis* (which due to their epithelial cilia move like living organisms) are easily infected.

Successful and unsuccesful attempts to penetrate produce, in the antenna, a local reaction caracterised by swelling and hyperaemia, which is easily appreciated, on account of the red colour of the blood in the larger *Planorbis*. This reaction is certainly due to the gland secretion, the inoculation of which must soften the tissue and help the miracidium in penetrating. The snails are generally indolent; when attacked by a larger number of miracidia, they try to retract the exposed parts or to leave the water.

This first reaction vanishes in a few hours, leaving at most one or more small nodules.

*Miracidia* which find no occasion to penetrateyin a snail, sink after some time to the ground and die, having first expelled the contents of the glands.

## Development of sporocysts of first and second generation.

(Figs. 18—50)

When an antenna of *Planorbis olivaceus* is examined shortly after the infection, the miracidium is seen stretched lengthwise under the skin; the intestine and the glands are indistinct and seem empty but the vibrating lamellae and the cilia of the external epithelium continue to play. Contractions and displacement of the miracidium are also perceived. Finally everything becomes quiet. The epithelium is cast off and there remains only an oval body with thin membrane, in which the germinative cells multiply and become more distinct.

(An antenna, cut off two days after the penetration of the *miracidium,* appeared oedematous. Immersed in physiological saltsolution and compressed by a coverglass, it became sufficiently transparent to permit the examination by an oil immersion lens. The sporocyst was still extended lengthwise, but on its outer side there was a clear space in which the rests of the ciliated membrane were seen. The cilia themselves had already disappeared leaving only indistinct rests. The outline was now very fine and the two poles were equal, as the papilla, the gland-cells withs their ducts and the great vesicular cells had disappeared. In the interior small granules, round bodies of nuclear aspect, vesicular elements and a few hyaline cells were seen in a protoplasmic mass without distinct structure. The four tubular orifices, with their ciliated membrane in lively movement, were still visible and continued so for at least five hours: also the ciliated epithelium of the antenna was well preserved, but after ten hours every movement had ceased; the epithelial cells of the antenna were detached and their cilia had dropped or disappeared.)

After three or four days the secondary swelling of the antennae indicates the evolution of the sporocysts. These simple or moniliform swellings increase in the first forthnight. About twenty days after the infection they become pale and shrunken without disappearing altogether; therefore the infected snails may be recognized even after a long time. But it must not be forgotten that similar lesions may be due to the parasitism of other trematodes.

After several days the distended membrane of the sporocysts has become so thin that it is hardly seen; nor may it be stained in the flattened antenna. Crushing one of the swellings 5-6 days after the infection, one sees a large number of round masses, formed by small cellules with a central body ressembling a nucleus. Some of them occupy the swollen part of the antennae, while others escape by the rupture. Examination in colored sections offers no great advantage.

A few days afterwards, the masses stretch, forming short secondary sporocysts that move about in the lymph of the antennae and for a short time in physiological solution. Constrictions are frequently seen, and seem to indicate a multiplication by transversal division. In water, they perish rapidly. In this period the emigration of the sporocysts towards the visceral sac begins. They are found there 20 days after the infection, forming very long and branched sporocysts containing oval masses, destined to the formation of new sporocysts or cercarias. In these the body is formed first, then appears the stem and finally the branches of the tail. The whole body is still covered by an epithelium with easily stained nuclei. Living and active cercariae appear only after a month and a few days. In other cases, due probably to less favourable temperatures, new sporocysts are apparently formed.

## Cercariae with forked tail. 7).

For some time past cercariae with forked tail have been known, though further evolution was ignored. They were considered as curiosites of no apparent importance. They are rarer in Europe than in warmer regions, where they constitute half of the easily found species. In Brazil, I know of four quite distinct species found in different *Planorbis*

(Figs. 65–68) and of one observed in a *Semisinus.*

In 1913 MIYAIRI and SUZUKI published an important work in which they described the evolution of the *Schistosomum japonicum.* The cercaria was found in a fresh-water mollusk with a shell like those of the genus *Bithynia.* It was considered new and called *Blanfordia* or *Katayama nosophora* ROBSON. The description and the illustrations show that the cercaria has six large unicellular glands in the posterior part of the body. According to the authors they are formed in secondary rediae which, however, are really sporocysts. The percutaneous infection was proved by experiments on animals.

The observations of the Japanese investigators were confirmed and amplified by independent studies, made by LEIPER. The latter, as chief of a scientific commission, continued his studies in Egypt where former students, though observing many cercariae, had failed to recognise those belonging to *Schistosomum.* He found four cercariae with corresponding characteristics and was able to obtain adult schistosoms in animals, as well by cutaneous infection as by ingestion of cercariae. As hosts of *Schistosomum haematobium,* he indicated snails akin to *Planorbis* and *Physa.*

Later on he concorded with the distinction between *Sch. haematobium* and *Mansoni* giving *Physopsis africana* as principal intermediary host of the first and *Planorbis Boissyi* as that of the second.

### Description of the cercariae of Schistosomum Mansoni.

(Figs. 48 & 51—63.)

The newly formed cercariae, found in great numbers in the viscera of infected snails, are covered, body and tail, by an epithelium with large and closely disposed nuclei, also revesting the suckers and making them stand out clearly. After this has been shed by a kind of moult, tke body becomes more transparent without showing its structure more clearly (Fig. 62).

Fresh preparations were fixed in osmic acid, others in formol and coloured by various methods; segments of infected snails were stained with hematoxylin only, or followed by eosin or VAN GIESON; thus I was able to verify the following details of structure which are not easily seen by using one method only.

The body of the moving *cercaria* shows the varied aspects, observed in other flukes and due to their extreme contractibility. In repose they assume the form of an egg with one end truncate. The greatest length is 0,14, the greatest width about 0,04 - 0,05 mm. The tail shows a very contractile basal part, forming in repose an elongated cone; fixed to its truncate apex is a spindleshaped transverse piece which can be folded in the middle, so as to form a prolongation of the basal part (fig. 60). This has a length of about 0,27 and a (greatest) width of 0,03, each half of the transversal piece being about 0,08 mm. long. Thus the whole length may attain nearly 0,5 mm. With good light, these dimensions are sufficient to show the stationary cercaria in the shape of a short white stroke. When swimming it appears in the very caracteristic form of an 8, due to the rapidity of its movement.

The whole body, tail included, is transparent, slightly opalescent and covered with very minute spines.

The body representing the earliest form of *Schistosomum* has two suckers, the oral one, with a diameter of 0,03 mm., being far larger than the posterior. Its shape is that of an ovoid with the anterior fourth cut off. Its musculary system is insignificant but the mouth and pharynx, situated at the posterior end may be drawn in the cavity and even reach the anterior opening. The movements of these parts are like those of the piston of a syringe and very striking.

Just inside the exterior opening of the sucker there is a ring of 6 or more small spines which, together with the supporting part, may be everted and form a short *rostrum.* Near their base open the excretory ducts of the abdominal glands, the secretion of which mav thus be inoculated in the tissues of the host. There are three ducts on each side, arranged like the strings of a cord (fig. 63). They perforate the anterior sucker and are so wide and sinuous that the abdominal part might be mistaken for a coecum The ducts are connected with six or more relatively enormous cells with granulated protoplasm, situated partly behind the ventral sucker and occupying a large space, characterized by transparency. They have a diameter of 0,03 mm, while that of the large nuclei is 0,01. The abdominal sucker with a diameter of 0,18 mm. looks very small; it is much nearer to the posterior end and may be retracted or protruded. Coloured preparations show behind the sucker an agglomeration of small and mostly elongate nuclei, other ones between the oral sucker and the large glandular cells and some round the suckers. The intestine is not easily distinguished; it seems to form a simple and short bag after the slightly visible, bulbless pharynx and oesophagus. Outlines of the genital system (which ought to be different according to sex) are hardly recognized. The numerous nuclei, seen in the cercariae, seem mostly connected with the muscular system; the others may belong to the glandular ducts, the nervous system, the intestine or the rudiments of the genital organs, but they are so little differentiated that in spite of much work I could not obtain a clear insight. The tail and its transverse piece are formed by nucleate cells of a certain size. It moves independently, even some time after it has been separated from the body, to which it is loosely attached by a kind of articulation.

After penetration the *schistosomulum* (fig 69) shows no more large glandular cell; they seem to vanish after having fulfilled their end. The ducts also seem to undergo involution; for the rest we find the same structures.

In this species the forked part consists of a separate spindleshaped piece at the truncate end of the tail. It may be bent in the middle so as to lie in the same axis or horizontally extended. This position is assumed while floating at the surface and supporting the body of the cercaria which hangs down. The extremities may also curl inwards (fig. 55). The comparatively small body and the rapid movement give to the cercariae, examined under low power, a certain likeness with spermatozoa.

Examination of infected snails show the cercariae formed in sporocysts, of which large numbers are found in in the liver and the genital gland. In the infected liverfollicles the glandular epithelium disappears; this explains the state of apathy and atrophy, so often seen in the infected snails. Of the infected *Planorbis*, the specimen, which lasted the longest, died after at three months, during which it furnished thousands of living *cercariae*. The production was diminishing towards the end of this period.

## Conditions under which the Cercariae leave the snails.

In the complete absence of light, the ripe cercariae do not seem disposed to leave their host, even at temperatures of 30 to 31 degrees, though they may accumulate in great quantities in the mucus expelled by snails. In the refrigerator, in intense cold and complete darkness, the free cercariae remain at the bottom of the water attached by the oral sucker; under these conditions they may live more than 24 and less than 48 hours. When the snail retreats into the shell, as it does before death, the cercariae do not come out, so that, after the crushing of a shell, hundreds of live cercariae may pass into the water which was before absolutely free of them.

Exposing the snails to the sun's rays for several hours, we obtain a great number of cercariae, so that experimental infections are preferably made between three and four o'clock in the afternoon. Bathing at this time must therefore be considered as more dangerous than in the early morning. Light alone, without corresponding heat, is not favorable to the coming out of the cercariae.

When the cercariae are active, they come to the surface of the water where they remain a long time hanging by the transversal part of the tail. When the water is shaken, they move rapidly, the body appearing in the form of the cipher 8.

In a capillary tube, placed on ice for a quarter of an hour, they retain life and movement; but they die in a few minutes in freezing water.

From three small snails that did not furnish any cercariae, an enormous number issued after the hosts had been exposed to rays of a NERNST lamp (without blue glass), until the right water temperature was reached. The diffused light of the mourning hours produced no effect.

Under favourable conditions the first free *cercariae* may be seen after little more than thirty days. At lower temperatures they appear later, which is probably due to the fact that the sporocysts form new ones in stead of cercariae.

In the beginning only a limited number of cercariae issues from the snails and spreads in the water and may easily remain unnoticed. As time goes on, they become more abundant and the swarming out may continue for some weeks. It is not easy to watch them in the act of emerging. I saw them several times issuing from the intestine, but this may not be the only way.

## Penetration of the Cercariae.

*Sch. cercariae* may reach their next stage in man or mammalia by penetrating through their mucous membranes while they are drinking or through their skin while they are bathing or staying in the water for some other purpose. Even the contact with hands or feet may be sufficient. The penetration is easy but its observation is difficult, even in experiments. However, it is clearly proved by the disappearance of the bodies of the cercariae from the water which was in contact, their presence in sections of the skin, reaction on the point where they penetrated and finally the appearance of adult blood flukes after a month or more.

LEIPER observed the infection of rodents and monkeys. In my experiments guinea pigs and rabbits gave good results. The cercariae seem to attack all the mammalia, exposed to them, but in many species the evolution does not reach the adult stage.

In experiments, partial immersion may be used or the animals may be gently but securely immobilized and part of the bare or shaved skin bathed by means of a wide glass tube containing the cercariae. After half an hour the water is full of tails which the cercariae cast off when they pierce the skin. The animals, principally white rats, show signs of irritation, followed for several days by local reaction.

When a piece of skin is removed twenty to sixty minutes after the bath the body of the cercariee may be found in sections. I obtained positive results in guinea pigs, rats and in a small pig which furnished the coloured preparation shown in fig. 69. The *Schistosomulum* is seen in the *rete Malpighii* the head touching the cutis. The glands are empty, as may be found even in specimens which just began penetrating.

The perforation of the mucosae ought to be much easier, but even the horny layer of the outer skin yields to the combined influence of glandular secretion and mechanical action. The cercariae do not choose the hair follicles or glandular orifices, as LEIPER already concluded from an experiment. made on a new born mouse. Here the penetration took place in ten minutes. However my experiments lead me to consider this time insuficient to warrant the perforation of the skin in larger animals.

## Evolution of Schistosomum in Mammalia.

The penetration is followed by a period in which the evolution of *Schistosomum* is little known. They probably soon reach the blood-vessels which carry them to different organs ; after a certain time they settle down in the portal system.

I obtained positive results in rodents, when many cercariae were used and some weeks allowed for the trematodes to attain a size which makes them easy to see. Without these conditions the research may give a negative result.

In rodents the development of a considerable number of *Sch. M.* is quite compatible with all the signs ot good health. The worms are evidently well adapted to life in the blood-vessels and their consumption of blood is not sufficient to cause serious anemia. The symptoms are mostly due to the laying of the eggs and their migration which only begin after some weeks.

In the excrements of infected guinea-pigs eggs were not found till after a period of 2 and 1/2 months and then only in small numbers. In the worst infection (in a rabbit) eggs were rare in the sub-mucosa and there were none voided; it may be that in man the conditions are different but, in the cases of rabbits and guinea-pigs, we may conclude that the elimination of eggs is a slow process and that it generally happens some time after the parasites have reached maturity.

Some observations in human pathology and some of the experiments of LEIPER seem to indicate that the elimination of eggs took place rather sooner, five or six weeks after infection. I think the fresh cases must have been very heavity infected and that later on the eggs would have been more numerous.

After three weeks adult worms are found in the mesenteric veins which are generally very congested. The veins of the liver contain about the same number. After five weeks the sexual organs are well developed; in the uterus the females show a ripe egg. The dimensions of the flukes vary considerably, according to the degree of muscular contraction. The specimens which die slowly in the tissues of the host, are quite relaxed. But even so the dimensions are slightly inferior to those given in the old literature. I do not think that this is due to the difference of the hosts, as the worms, found in autopsies of infected people, were not distinctly larger, but perhaps the species *Mansoni* may be smaller than the *haematobium* of which the females contain many eggs, instead of one only. The intestine of the female can be easily seen, as it is full of black matter, formed from the absorbed and digested blood. The same may be said of the male though in a lesser degree. In sections of the liver, the females, cut transversally, would be little conspicous, if they were not characterised by the intestinal lumen showing in one or two places, according to the region. Besides this, the sections of the excretory canals are seen. The male is more characteristic, due to its form and to the spines on its body.

### Symptomatology of Schistosomatosis.

There are several methods for determining the symptoms of infection by *Sch. Mansoni.* We can study men (naturally) and animals (experimentally) infected with the disease, verifying the objective symptoms and taking note of the complaints of the patients; or we may begin with the macro-and microscopic anatomic alterations. Whe have another resource in the comparative study of the lesions, produced by other species of *Schistosomum* in men and domestic animals. The most important is the *Schistosomum Japonicum* producing very intense infections, as well in man, as in the larger domestic animals. They are generally located in the same organs and have been widely studied 9).

The first observations on *Schistosomum* infections, made in the Old World, may be used but only with great caution, as the symptoms belonging to two species of *Sch.* and other intestinal parasites are frequent in the same place.

The presence of adult worms in the veins is mostly well borne (which agrees with the general rules of parasitism); it is proved by the fact that a rabbit may have half a thousand worms in the mesenteric veins without showing any particular symptoms.

On the other hand, LETULLE attributes the phlebitic processes, observed in cases of long standing, to the parasitism of the adult.

Glands with toxic or irritating secretion are unknown in adult schistosoms, but certainly the products of their metabolism are poured into the circulatory system of their host 10). They are however diluted and carried along when the circulation is free, as in the larger, veins. The blood, absorbed by the schistosoms, is their only alimentation but it is not so much that in moderate infections, it could not be easily. substituted For this reason anemia is no help for recognising the infection. People often attribute diarrhoea to the parasitism of worms and some authors, amongst them GONÇALEZ-MARTINEZ, consider it as a symptom of the infection of *Sch. Mansoni.* According to my experience, it is only a frequent complication, as in other worm diseases and in chronic cases one finds habitual constipation which is explained by the sclerosis of the intestine. In recent cases the number of stools is generally not increased.

JESUS-RISQUES called attention to undefined pyrexy of uncertain origin which may be attributed to *Sch. Mansoni* infection 11).

I was present at the autopsy of a patient infected by these parasites who succumbed to a not very characteristic pyrexy. This subject is worth considering. It is already proved that acute and recent infections of *Sch. Japon.* may cause fever which is often acompanied by eruptions somewhat resembling urticaria.

There is another symptom, which in my experience, is more frequent and which may be explained, taking into account the anatomical observations made in patients, infected by *Sch. japonicum* and *M. pulmonalis.*

These patients often complain of gjddiness which I attribute to the embolism of the blood flukes or their eggs.

Some patients, who were accustomed to bathe frequently in ponds, told me; that they felt itching afterwards. Even the name of two of the ponds, we visited, refer to the itching. Though this symptom may not be considered pathognomonic, tt always gives a pretty sure indication of infected water and leads us to expect penetration of cercariae, which causes irritation, as is well seen n the experiments on white rats 12).

There is a series of symptoms, observed only in cases of intense or often repeated infection, which concern the intestine and the liver and which are explained by the anatomical lesions, observed in those organs.

These, however, depend rather on the eggs than on the worms, the eggs being deposited in the tissues, as we shall see in the pathological anatomy. The symptoms of the liver and intestines are, however, not very characteristic and may be found in many other affections; so their value depends on the exclusion of other complications or accidental diseases, observed in infected individuals who, in some places, form the majority of the population. The frequency of certain symptoms might be demonstrated by statistics but in this line nothing has been done in this country 13).

Sanguinolent mucosities may be attributed to *Sch. Mansoni,* if there are many eggs and no amoebae. Icterus, hepato-and splenomegalia, retraction of the liver and ascites are also suspicious symptoms when there is no probability of other etiology.

Eosinophilia is observed in schistosomatosis as in other forms of helminthiasis, without being of much importance for diagnostical purposes, as the greater part of the patients have also other worms. It is rather by an examination of the fecal matter than by one of the blood that a reliable diagnosis may be obtained, excepting only cases of quite recent infection.

The other affected organs do not furnish any clear symptoms. In the first phases of their evolution, the worms probably pass through the pulmonary circulation; some not very characteristic manifestations, such as bronchitis and cough, may be due to them. The pancreas is often affected; it is advisable therefore to seek for indications of glycosuria, which has not yet been done systematically.

Besides the attacks of giddiness, nervous perturbations are observed which may be due to schistosomatosis; these are lapse of memory, want of energy, feeble comprehension and reasoning, periods of apathy and bad temper, etc.

**Complications and secondary affections.**

Infection with *Sch. M.* is so common that the coincidence of other pathological conditions must necessarily be very frequent. Thus liver abcesses may be due to *amoebiasis* and may be attributed to the schistosoms, simply because their eggs are found. *Appendicitis* of other origin may take place in an appendix, infiltrated with eggs. Even symptoms which are generally observed in *Schistosomum*-infection may be partly due to complicating conditions, as tuberculosis, syphilis, alcoholism and heart diseases. In severe affections of the rectnm (which seem particularly frequent in Egypt) the *Sch. haematobium* may be partly responsible. Haemorrhoids may be altogether independent or a consequence of *cirrhosis hepatis*. Anal fistule may be independent or due to mixed infection. (I dont know of any attributable to *Sch. M.* alone). Adenoms and papilloms, found from the ileum to the rectum in increasing number, may be due to intense and long standing infections but the malignant degeneration of them ought to be considered a complication. *Haemoptysis*, observed in chronic cases, may be dependent on other causes.

On the other hand the parasitism of *Sch. M.* may favour complications and secondary affections. It certainly proves the existence of sanitary conditions which favour an infection, not only by other worms but also by protozoa and bacteria.

**Pathological anatomy.**

The results of the parasitism of *Sch. M.* are better unterstod by macro-and microscopical investigation of the anatomo—pathological conditions than by the symptoms, observed in life. These results allow us to approach certain questions which are still somewhat obscure. I shall first state my personal observations made on animals experimentally infected.

In rabbits, guinea pigs and white rats, the presence of the blood flukes is hard to prove during the first period after experimental infection, evidently, because they have not yet reached their final habitat. This agrees with the results of other helminthological experiments. The youngest and smallest specimens were found by LEIPER in the liver of white rats.

After three weeks, we may count with positive results. On opening the animal, the mesenterial veins are full of blood and the tissues are so transparent that the males are easiey seen, their white colour being in contrast with the surrounding blood. They are found in all the larger branches, from the stomach to the end of the intestine, without any preference for the last part. By dilaceration of the liver in physiological salt solution, a similar number may be obtained. The females are found in about equal numbers with the males occupying their *canalis gynaecophorus* but after some time the sexes separate.

In recent infections, the veins, although full of flukes, show no distinct lesions. The neighouring tissues, the liver and the intestine are free from macroscopic alterations.

Complete development and egg production require one or two weeks more. Even in heavy infections the eggs do not appear immediately in the excrements which shows that their emigration is slow.

After many months the larger veins may be found empty, but sections of the liver and the intestine show some males and many females, isolated in the smaller veins.

In the liver the females are found in the small interlobular veins, more rarely in dilated capillaries or small arteries, never in bileducts or in the glandular tissue. The bloods vessels seem very congested but there is no inflammatory reaction around them. In the inicial time, eggs in liver preparations are rarer than sections of flukes but they are often surrounded by an infiltration of round cells. In severe infections of older standing the whole interstitial tissue may be thus infiltrated, which may be considered as the first stage of a cirrhotic process. The capillaries seem much distended.

In the intestine I found the males near to the serosa; the females can reach the submucosa. The eggs are found in small groups in the mucosa at the base of the glands and also isolated between them, but sparsely and without indicating, how they reach the surface. The groups of eggs are surrounded by an infiltration not unlike a tubercle. Giant cells are formed exclusively arround or inside of the empry shells. Eosinophilous cells are seen in the tissue and in the vessels. In older infections the eggs may also abonnd in the submucosa.

On the lesions observed in man much has been written. The first writers did not distinguish between the two infections found in Egypt and most of the older or newer authours treat in preference of fatal cases where the infection was many years old. In such cases, in the sections the flukes may be rare or even absent. The predominant lesions are due to the eggs which exist in large, often enormous numbers. Small lesions without great importance, when constantly repeated, lead finally to severe and extensive lesions of the most invaded viscera.

Material from early stages is rare. However, I have elements for describing them, using personal observations and others found in the litterature.

Of macroscopical lesions the only ones, observed in more recent and not very severe infections, were a swollen spleen and medullary tumefaccion of the mesenteric lymph nodules, both very common in other diseases. The flukes are not seen in the mesenteric veins and the best places to look for them are the trunk and the ramifications of the portal vein.

In older and more severe infections there are lesions of the liver which may look either like hypertrophic or like atrophic cirrhosis and may cause ascites and jaundice 14). The spleen which as a rule is free from flukes and eggs may be swollen or small. Of other organs only the intestine shows striking alterations. They may consist in a varying degree of general sclerosis and alterations of the mucosa, more apparent in the rectum and diminishing in proportion of the distance from it. The difference in localisation between man aud animals may be due mostly to gravitation.

The histological alterations of the organs were studied in my material and also in preparations received from Dr. J. RISQUES in Venezuela and compared with good preparations oi infections with *Sehistosomum japonicum.* Some were from human infection, made by Prof. CROWELL in the Philippines and others from domestic animals, received from Prof. AKANASCY. The infections were severe and the corresponding lesions were well accused.

Individuals, who suffer from infection with *Sch. M.* beginning in early youth, may show few flukes in comparison with the enormous number of eggs, accumulated in the tissues, without the slightest probability of leaving them during the life of the host. They are more numerous in the liver and the wall of the intestine, but are found also, though in smaller number, in other organs, as the mesentery and its lymph glands, the pancreas, the lungs and the brain. Like the eggs of *Sch. japon.* they are often found in the interstitial tissue of the viscera, independent of any celular infiltration; they may be more or less calcified which points to their staying there for a long time. Such deposits are the cause of the sclerotic process, found principally in the terminal part of the gut and in the liver, where they lead to a form of cirrhosis, with or without splenomegaly, jaundice and ascites.

The intestinal sclerosis impares the funtion and leads to obstipation. Though most pronounced in the rectum, it extends upwards and there are many accounts of thickening of the appendix, due to infiltration with eggs. It may even extend to the higher parts, though it does not call the attention of the observer.

Macro— and microscopic lesions of the intestine where studied accurately by LE-

TULLE in a case from Martinique, infected most likely by *Sch. M.* only, though the author speaks in somewhat vague terms of the coexistence of eggs with terminal spine. His descriptions agree with those of the authors who observed very severe cases and some of them may be found also in less intense infections. Similar lesions may also appear in *Sch. japon.* infections which are frequently severe.

LETULLE describes superficial ulcerations of the mucosa, different from those dependent on amoebiasis. In other places he noted a proliferation leading to the formation of polypoid pedunculated growths with the caracter of adenoms. They might be traversed by a fibrous axis and have an ulcerated surface.

LIEBERKUEHN'S glands may be destroyed by ulceration, atrophy or cystic dilatation, followed, suppuration, or become hypertrophic or hvperplastic. The epithelium shows the corresponding alterations without undergoing a typical proliferation.

The interstitial tissue of the mucosa also shows signs of, sometimes extreme, hypertrophy The capillaries may appear numerous and distended, while the interstitial tissue may force the glands assunder and spread on the surface of the mucosa, below the epithelium when it still exists. Interstitial hemorrhages and pigment deposits were never seen.

The muscularis mucosae is not reached by the ulceration nor does it show other alterations than hyperplasia.

The submucosa is transformed into sclerotic tissue, while the adipose cells disappear.

The layers of the muscularis propria only show general hypertrophy, real or apparent.

The serosa was also sclerotic in LETULLE's case, but the products of parasitism, observed in other cases, were not seen.

The lymph vessels show no alterations, except some cellular infiltration near to the foci of inflammation and ulceration. They are not used for the migration of the worms and eggs. The lymph follicles are not invaded by the parasitical process. Also the nerves and ganglia show no lesions.

Except in the parts which pass through the muscular layers, the veins undergo a special and characteristic process of hypertrophic and sometimes obliterating endophlebitis. The remaining free space is generally excentric, the process being limited to part of the intima. It may be seen alo on the mesenteric vessels and in the veins of the pelvis, which do not properly belong to the portal circulation. A hyperplasia of the media is also noted here.

## Oviposition and migration of the eggs.

The main questions are: How do the eggs reach the extravascular tissue and how do they arrive in the intestinal contents? The solution of these questions is very difficult but seems to have hardly troubled most of the authors. Following LETULLE, they took for granted that the females advance in the small veins until they plug the narrower vessel, and then depose their eggs in them. They think that the increased pressure, following the plugging of the veins, forces them through the wall, and that afterwards they make their way to the diffent places were they are found. As for the eggs found in the luugs, in the brains etc. they were supposed to be carried by the bloodstream.

What may be the force which makes the eggs, relatively large and motionless bodies, advance in the tissues? Here the authors evidently thought of the eggs with terminal spines, which might help the progress in one direction while the other blunt end prevents a retrograde movement. But the lateral spine would not help the advancing, while it might oppose any motion in which the spineless end does not go first. And the eggs of the *Sch. Japonicum* have not even got a spine. It is true that a diminutive thorn has been described, but it is generally not terminal and is often missed altogether, as well in preparations from stools, as in preparations from tissues. It seems far from constant. Also the point is often curved and generally not very sharp.

Nobody seems to have considered, that it would be much easier for the worm to perforate the wall of the vein and pass through it, if not with the whole body, at least with the anterior part, also the position of the genital opening and the analogy with other worms suggest this idea. The very endophlebitis speeks for it, as it is always excentric (even when almost obliterating) and thus indicates a localized lesion.

It is true that this process of oviposition has not been witnessed in the preparations, as far as the literature and my experience go, but neither has the oviposition in the vein.

It is easier to unterstand how the eggs, which are so often seen at the base of the mucosa, may come to the surface, though the bloodstream in the veins and the lymphcirculation go in the opposite direction. They generally follow the tissue between the glands of LIEBERKUEHN and do not pass through them (as the preparations clearly show). The only force acting in this direction is the reconstitution of the tissue. No abscess formation helps the elimination and the ulcerati ons, when present, are quite superficial. I cannot share the opinion of LETULLE, who thinks that the dilated and sometimes suppurating glands, help the escape of eggs and miracidia, nor can I admit that all the living eggs should have passed through the warty or pedunculated adenoms which are found in old cases. They are more likely to be the source of the degenerated and calcified eggs which are abundantly found in the stools of certain cases.

As for the eggs, seen in the submucosa and under the serosa of the intesiine, in the liver, pancreas, brains and lungs, they mostly fail to reach the surface in a living state, as long as the host is alive. They accumulate in the tissues, where they are seen in great numbers, and, after provoking during a short period an inflammatory reaction, they finally are incapsulated in a cicatricial tissue without a sign of reaction. Calcification sets in after an indeterminate, but probably very long, period and may indicate the final death of the egg.

Living eggs are not known to have been found in the bile or pancreatic secretion. I examined the contents of the gallbladder several times with constantly negative results. In sections the eggs are never seen in the bile ducts.

Other worms are known to deposit their eggs in the tissues of their hosts, for instance the *Hepaticola hepatica*, the eggs of which are very common in the liver of the common rat and have often been taken for coccidia. In this case it is quite sure that they are deposited by the adult worm which afterwards dies in the same place. The eggs do not reach the outside world, unless the host is eaten by any animal or dies in some other way.

Besides living eggs in their earlier stages and calcified ones, the tissue may contain empty shells, as the typical form of the tear and giant cell formation clearly show. They are found in different situations and not only near to LIEBERKUEHN'S glands, as might be supposed from LETULLE'S description, who considers the escaping of the miracidium by the hollow space of the gland as a normal way of spreading the infection. We may state that neither he nor anybody else ever saw a free embryo in the sections. In my opinion it is extremely unlikely that miracidia, escaping from the eggs in the tissues, should pass through the intestine alive and, even so, they would die soon, unless they came immediately in contact with water. I cannot believe that the rather rare ocurrence of ecdysis in the tissues is of any advantage for the propagation of the flukes, but the fact is very interesting and hard to explain.

Undoubtedly in the infection with schistosoms as well, as with many other worms, there is an enormous waste of eggs which in our case is not even compensated by a large production. The real compensation is given by the enormous multiplication in the organisms of the infected snail.

In the larger number of cases the ripe eggs appear mixed and in close contact with the common elements of the stools and not involved in bloody mucus. This constant output not only insures the conservation of the species, but indicates the existence of a relatively quick and easy way of leading the eggs to the outside world without striking symptoms. Thus the facility, with which the infection is overlooked, may be understood.

## Prognosis, Therapeutics and Prophylaxis of Schistosomatosis.

From our observations already refered to, one may conclude that in our country schistosomatosis is mostly not severe. GONZALEZ-MARTINEZ estimates that 45 % of the infected show no clear symptoms and I think that in Brazil the proportion of unremarked cases is rather higher than lower. On the other hand I dont know of any treatment for curing or improving this infection 15), while some of my observations show that these flukes may live for many years in the human body. Therefore our principal efforts must be directed to the prevention, rather than to the cure of this infection.

Schistosomatosis is always dependent on water, either used for drinking or coming in contact with the skin. As its infectiveness is necessarily connected with the presence of certain species of Planorbis, it is evident that prophylaxis ought to be directed in the first line against these intermediary hosts. The water collections might be cleaned by removing mud and aquatic vegetation and catching the specimens in sight, but these measures will be often difficult or impossible just there where they are most needed.

There are other measures for preventing the infection of the snails, which would also tend to eradicate the even more common and dangerous *ankylostomum* and *necator* infections. They are directed against the contamination of soil and water by human excrements. It is clear that sewers opening into rivers, the water of which is used for bathing and washing, could not be tolerated.

If suspect water must be used, a storage for 24-48 hours would be a sufficient protection. Early in the morning the water is not likely to contain cercariae; taken near to the surface and stored for a few hours it will lose any power of infection. The same may be achieved by heating (which need not attain the boiling point) or by desinfection. According to LEIPER it is sufficient to heat the water up to 50 % or add one gramme of sodium bisulfite to the liter.

## The danger of bathing in stagnant water.

Planorbis (of the larger species) are found in waters with little or no current, not subject to complete evaporation and preferably with floating or rooted water plants Such waters may be dangerous, when drunk, but would be avoided, when there is a choice in the supply of drinking water. But already the contact with the bare skin of legs and arms, as in fishing and washing, may cause more or less severe infection; however the greatest danger consists in total and prolongated immersion while bathing, as the chances of infection increase in proportion to the surface exposed and the time of contact. I know the history of several patients who were in the habit of bathing in stagnant water with water plants and *ampullariae.* These much larger snails are eatable and better known; they may thus serve as indicators for suspect water. A few patients had even noticed the presence of *Planorbis.* In some places, for instance in Aracajú, *Planorbis olivaceus* may become so abundant in dry times that it is used for feeding pigs. There and also in Laranjeira, we found ponds, whose popular name indicates that people who bathe feel itching afterwards. This is quite a caracteristic symptom of the penetration of the cercariae, as experiments in animals, principally in white rats, clearly show.

To become infectious the water collections must be contaminated with *Sch.* eggs coming from the intestine of man or animals. This may happen at any time but mostly in consequence of showers and inundations. Of course the water must also contain specimens of *Planorbis.* At a sufficiently high temperature, after 4—5 weeks, there may be infected snails in condition to furnish living cercariae for two or three months. Thus a contamination, taking place every second month, would be quite sufficient to make the water permanently suspect.

We know by experience that the cercariae dont issue at any time. It is next to impossible to find a cercaria early in the morning, though the water may contain infected snails, while in the afternoon, after several hours insolation, they are quite abundant. Therefore a short bath in the morning may prove harmless, while a protracted bath during or after the warmest hours ma leady to a multiple infection. The dry season, when there is more sunshine and less water, while its temperature is higher, must be the time when most of the infections are acquired.

## Litterature:

The litterature on the blood flukes and the pathological conditions caused by them is very large; LEIPER's report contains an alphabetical list of 562 numbers. A few more may be found in other papers cited. I give a list of papers which refer specially to my subject and principally of those which have been studied and quoted. I have not enumerated the numerous treatises on helminthology, tropical diseases or general pathology and medicine, as they are generally well known or contain nothing new.

The litterature on *Sch. jap.* is given more extensively, as the subject is new and intimately connected with mine. Not only do *Sch. M.* and *Jap.* provoke similar symptoms and lesions but those of the latter are generally better known and more easily studied, the infections as a rule being less complicated, more acute and more intense. Therefore their study is very useful to the student of *Sch. M.*

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# VI

## Schistosomum and allied genera.

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# VII

## List of Litterature.

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## Notes.

1. (Pg. 108 after the title.) The helminthological and malacozoological litterature used for my studies belonged to me or to the libraries of our institute and of the *Museu Nacional.* A large part was seen only after the termination of my first studies, begun in the second trimester of 1916 and published in the Brazil Medico in two preliminary communications. The historical and geographical notes were compiled from

this literature. The parts which refers to the parasite and its evolution gives my personal, indepent and generally repeated observations, accompanied by original drawings. Where the work of the commission under LEIPER had already cleared the ground, my personal observations agreed in all the essential points. The part refering exclusively to the local conditions in Brazil is my own. The serial sections used for this paper came from more than fifty blocks and were mostly made in the anatomo-pathological laboratory of this institute, then directed by Dr. OSCAR D'UTRA, and some by Dr. TRAVASSOS of this institute. They were examined by me, as all the others, made in my laboratory without the use of paraffininclusion. The patients who furnished the material for the numerous infections of snails, made by me, were sent by Dr. OSWINO PENNA, after he had observed eggs of *Sch. M.* in their stools.

The *Planorbis olivaceus*, used in my studies, were brought from Aracajú by THEOPHILO MARTINS, sent by the institute, or received from Bahia through the kindness of Prof. PIRAJÁ and Dr. OCTAVIO TORRES. When studying the fresh water shells, I compared the collections in the musea of Rio de Janeiro aud São Paulo.

These studies occupied a great part of my time during more than two years (with many interruptions due to want of the necessary materials). They were helped in many ways by the directors of this institute Drs. OSWALDO CRUZ and CARLOS CHAGAS. To them and the other colleagues already mentioned my best thanks are given.

In 1917 this paper was practically concluded and the plates were ready, but printing was adjourned in order to present the work at the medical congress held in Rio in October 1918. The essential part was read in a lecture, accompanied by projections before an audience, already somewhat reduced by a sudden epidemic of influenza. This and other circumstances further delayed the printing. Since this time only a few additions have been made, in connection with the more recent literature.

2. (Pg. 109, l. 6 from the bottom of col. 1.) *Schistosoma*, derived from σχιστός split and σῶμα body, is the Greck name for the worm and this gives *Schistosomatosis* as correct form.

3. (Pg. 110, l. 11 from top of col. 1.) The blood fluke named by SAMBON *Schistosomum Mansoni* is a good example of the difficulty of nomenclature. The generic name of DIESING is not only more caracteristical but really anterior, though the record of the session in which it was announced, was published after the first paper of WEINLAND. The name of *haematobium* included two species, of which one was first considered new by HARLEY who named it *capense*. It seems to me that this name ought to stand. If the author did not recognize that his speies was part of *haematobium*, he had the excuse that the double shape of the egg in the same specimen of the egyptian blood fluke was considered established by an observation of BILHARZ. This observation, used as principal argument by the unitarian, was most probably erroneous, as may be easily supposed when we take in account that *Mansoni* has only one egg with shell. It has not been confirmed by any recent author and is invalidated by countless observations. If the name of HARLEY holds good, then the name of *haematobium* must be restricted to SAMBON'S *Mansoni* and might mean both species or each one of them. This might be prevented by suppressing the name *haematobium* and distinguishing between *capense* and *Mansoni* but this would be considered incorrect by many and would substitute a little known name for another already much used. In this emergency I shall continue to use the uame *Mansoni*, while the form with an apical spine on its egg wonld be *haematobium* (forma *capense*).

4. (Pg. 111, l. 7, from the top of col. 1.) *Schistosomum* and allied genera in mammalia and birds: There is a considerable number of species which I enumerate in chronological ordre with their synonyms.

1851 *Schistosomum haematobium.* Man and other mammalia.

1854 *Distomum canaliculatum* RUD. (=*Ornithobilhazia* de ODHNER) in spec. of *Larus* and *Sterna.* Found in Brazil by NATTERER, reobserved more than twenty years ago by LUTZ in Santos and since in Rio by FARIA and TRAVASSOS.

1864 *Distomum capense* HARLEY (=*Sch. haematobium* ex parte.)

1876 *Schistosomum crassum* (SONSINO) In cattle and sheep, Africa, Sicily and Sardinia.

1895 *Bilharziella polonica* (KOWALEKY) In ducks. Europe.

1904 *Schistosomum japonicum* KATSURADA. Man and other mammalia.

1907 *Schistosomum Mansoni* SAMBON (*Sch. haematobium* ex parte).

1906 *Schistosomum spindale* MONTGOMERY. Bovidae. India. Sumatra.

1906 *Schistosomum indicum* MONTGOMERY. Bovidae. India. Sumatra.

1906 *Schistosomum bomfordi* MONTGOMERY. Bovidae. India. (France).

1916 *Schistosomum turkestanicum* SKRJABIN. Bovidae. Turkestan.

There are a few more species in birds like *Gigantobilharzia acotyla* ODHNER 1910, *Ornithobilharzia intermedia* ODHNER from European *Laridae* and *Kowaleskii* PARONA from *Larus melanocephalus* in Europe.

These blood flukes form a group of digenetic trematodes to whicch some authors give family value, calling them *Schistosomidae* or *Bilharziidae.* They were discussed under this name by ODHNER (Zool. Anzeiger 1913, p. 58).

5. (Pg. 111, l. 15 from top of col. 1.) V. HOLCOMB 1907. A quite likely explanation is that the female of one species might be carried by the male of the other to its place of predilection thus causing an abnormal localisation of the female.

The terminal prolongation of some eggs of *Sch. m.* (fig. 11) may also be erroneously taken for a spine.

6. (Pg. 112, l. 17 from top of col. 2) I saw this swamp in its natural state which seemed favourable for the breeding of aquatic molluscs. Dr. COSTA LIMA who directed the drainage stated to me that the workmen always accused itching after having entered the water.

7. (Pg. 115, l. 9 from the bottom of col. 2.) After my work was finished I received two interesting papers by WILLIAM CORT (Univ. of Calif. Publ. in Zool. XVIII, No 17 & 18, Jan. 4, 1919) on the Cercaria of the *Sch. japonicum* and the eggs and miracidia of the other human blood-flukes. In the first paper the author represents the excretory system with its ramifications, the nervous system and a cephalic gland inside of the oral sucker and the rudimentary intestine in very clear (but evidently very schematic) drawings which makes the comparison with *Sch. M.* rather difficult. The second paper contains two microphotographs and five drawings of the eggs and miracidia of *Sch. M.* and *Sch. japooicum.* It is interesting to compare the want of details in the photographs with the distinctness of the drawings (which illustrate the interpretation of the author but hardly resemble the aspect of the microscopical preparations). I call attention to the fact that in his two first cases the author failed to find the rudimentary spines on the eggs of *Sch. jap.* In a third case they were found in varying size but only in one half of the number examined. The author also gives historical notes and a list of publications.

8. (Pg. 120, l. 13 from the bottom of col. 1.) On the relation between the terminal-spined and lateral-spined eggs of *Bilharzia* Brit. Med. Journ. March 18th 1916, p. 411. "In the form derived from *Bullinus sp.* the males have four or five large testes and the two lateral gut branches are late in uniting, so that even when mature the worms have a short intestlnal coecum. In the female the ovary lies in the latter half of the body. The uterus is very long, voluminous and contains many terminal-spined eggs some of which lie

in pairs. The yolk glands have a limited range in the posterior fourth of the body. These worms belong to the species *Schistosoma haematobium* (*sensu stricto*). In the worms derived from *Planorbis Boissyi* the males are small and have eight small round testes. The two lateral gut branches unite very early. In some of the smallest specimens found this union had already taken place. The intestinal coecum is correspondingly very long. The female has the ovary in the anterior half of the body. The uterus is very short, and almost invariably there is only one egg at the time in each specimen when a number have already been laid. The yolk glands are extensive ranging through the posterior two-thirds of the body, along the whole length of the coecum. The eggs always have a lateral spine, the first laid is smaller than those succeeding and the spine is then set almost at right angles to the axis. Pending a consideration of the claims of other names to priority the speciffic name *Schistosomum Mansoni* may be adopted rightly for these worms. They differ in their adult structure from *Schistosoma haematobium* (sensu stricto) more markedly than does *Schistosoma bovis*.

Vesical bilharziosis and Manson's intestinal bilharziosis are therefore etiologically properly regarded as entirely different diseases".

9. (Pg. 123, l. 18 from the bottom of col. 2.) The study of the literature on *Sch. jap.* shows that the disease due to this blood fluke is generally more acute, intense and severe. This is easily understood as the production of eggs is much larger. Also the use of human excrements for fertilizing, the cultivation under water and the prolonged exposure of the workers in flooded ricefields favour intense infection, so that there is no need to suppose a greater virulence of the parasite.

10. The rests of the digested blood must be rejected by the mouth, as in all the trematodes without anus. We also find principally in severe experimental infection of animals black masses as well in the blood, as in the leucocytes and phagocytes in the tissue. They are also seen in human infections where however they might be taken for malarial pigment which in the laboratory animals may be excluded.

11. (Pg. 124, l. 1 from top of col. 1.) Lately (1918) LAWTON described an epidemic of fevers, observed in Australian soldiers, infected in Egypt. The symptomatology was very much alike with that of intense and acute infections by *Sch. jap.*

12. (Pg. 125, l. 1 from the bottom of col. 1.) We have in the institute a film showing a white rat, after prolonged immersion of the posterior part of the body in water with many live cercariae. The itching principally in the hind feet and tail is charactically shown by the biting of these parts.

13. (Pg. 124, l. 19 from the top of col. 2.) I record here that in the acute infections, cited in note 11, there was cough, accompanied by evident symptoms of bronchitis and pulmonary congestion. The sputa sometimes contained blood. These are early symptoms of infection. Later ones might be due more to the eggs than to the worms.

14. Microscopical preparations of spontaneous infection with *Sch. Jap.* in the large domestic animals show distinctly the latter lesions, cirrhosis of the liver and alterations in the veins.

15. Considering that anthelmintyics may not reach the flukes in the portal circulation, unless extremely diluted, other remedies were tried, such as arsenical and antimonial compounds, emetine and methylene blue. However, these substances although useful in infection, by protozoa, spirilla and allied organisms, dont seem to promise much result when used against blood-worms. Even if they killed the flukes without producing new and perhaps even more serious symptoms, there would still remain the eggs and the lesions caused by them, unless the infection was quite recent and therefore not easily recognized. Several authors claim good results, but such ought to be demonstrated by animal experiments which are easily made. LEIPER who

proceeded so, failed to get good results. The literature of this question may be found in a thesis of ELPIDIO DE ALMEIDA, just published (1919).

*Additional Note* (Jan. 1920): CHRISTOPHERSON published several papers on the treatment of *Schlstosomum* infection by Tartrate of Antimony. One of them, iu collaboration with J. R. NEWLOWE, appeared in the Journ. of Trop. Med. V. XXII, pg. 128, 1919 and refers seventy treated cases. He declares that the results were very good and were partly controlled for two years. The author mentions mostly cases of *Sch. haematob.* and recommends a dose of 25—30 grains, approximately 2 grammes. The first injection contains 1/2 grain in 3 ccm. of physiological salt solution. (The injections are made in a vein.) This is repeated every second day, always increasing the dose by half a grain, till 5 grains are reached. After some days the blood disappears from the urine and the eggs become sterile about two weeks after the dose of 20 grains has been reached.

These results want more confirmations refering to patients with *Sch. M.* One experience we made in a guinea pig shows that a cure cannot be obtained by a few large doses. The treatment must be necessarily rather long, when made by this method, and may not be shortened, as the drug must be used with precaution.

## Explanation of Plates.

**Plate 37 (Figs. 1—8).**

Fig. 1 ♂ & ♀ of *Sch. haematobium.* The ♀ contains many eggs with terminal spine.×28. Copied from FRITSCH.

« 2 ditto. The ♀ shows the intestine double till near to the caudal end. Copied from BILHARZ.

« 3 ♂ & ♀ of *Sch. Mansoni.* The balsam-preparation shows clearly the bifurcarted intestine which in both sexes unites before the middle of the body.×50. Orig.

« 4 ♀ of *Sch. M.*, first third of the body, showing only one egg with lateral spine.×40. Haematoxylin stain. Orig.

« 5 ♂ of *Sch. M.* showing the testicular apparatus.×20. Orig.

« 6 Another ♂ of *Sch. M.* showing the same in three different positions.×60. Orig.

« 7 a, b. Two ♂♂ of *Sch. M.* showing the common appearance of eight testicular lobes. No sign of a vesicula seminalis.×60. Orig.

« 8 of *Sch. haematobium* copied from BILHARZ.

**Plate 38 (Figs. 9—38).**

Fig. 9–14 Abnormal eggs of *Sch. M.* 9–11 Shell with protruded anterior pole, liable to be mistaken for a terminal spine; 12 egg with two spines; 13 crystals deposited on egg shell; 14 calcified egg. ×150. All the eggs were voided by patients infected in the north of Brazil.

« 15 Normal egg of *Sch. M.* showing the embryo.×400.

« 16 Miracidium observed some time after ecdysis.—Stained preparation.×400.

« 17 Miracidium which failed to penetrate a long time after ecdysis.×400.

« 18 Miracidium attacking the antennae two have already penetrated.×200.

« 19 *Planorbis olivaceus* with normal, 20 & 21 with infected antennae. The specimens are halfgrown. Natural size.

« 22–38 Aspect of antennae in various degrees of infection. Figs. 19–27 in nat. size, 29-38 somewhat enlarged. Fig. 32 shows a normal antenna. All the drawings are original and, with exception of 32, taken from fresh or living specimens.

**Plate 39 (Fi s. 39—47).**

Fig. 39 a young sporocyst inside of the antenna showing the 4 tubular orifices with vibrating membrane and the ciliated epithelium half detached, b the same more developed with initial state of secundary sporocysts.×100.

« 40 Almost mature primary sporocyst, the young second generation escaping through a tear of the antenna under compression.×150.

« 41 Section through an antenna containing an aimost mature primary sporocyst. Haematoxylin staining ×150.

« 42 Secondary sporocyst.×500.

« 43–45 Secondary sporocysts, more developed, from the internal organs of Planorbis. Lateral illumination.

« 46–47 Ditto, seen by transparency. All the drawings are original and taken from fresh preparations, with exception of 41.

**Plate 40 (Figs. 48—63).**

« 48 Section of liver of an infected Planorbis showing an almost ripe cercaria in longitudinal section- Stained preparation.×250.

« 49 & 50 Ditto showing cuts of secondary sporocysts.×700.

« 51 Living cercariae of *Sch. M.*×30.

« 52–61 Cercariae of Sch. m. from various preparations. ×120.

« 62 Living cercaria. The drawing is combined from various.

« 63 Stained section showing the twisted excretory ducts and the superior gland cells in oblique cut.

Plate 41 (Figs. 64—70).

Fig. 64 *Dicranocercaria ocellifera* alive ×60

« 65 Ditto stained (glycerinpreparation). ×250.

« 66 Ditto unstained ×250.

« 67–68 *Dicranocercaria valdefissa*. Unstained preparation ×250.

« 69 Section of skin from pig showing a penetrated *Schistosomulum*. Stained preparation. ×600.

« 70 Intestinal loop of infected guinea pig showing mesenteric veins dilated and full of flukes. Formolfixation. Natural size.

Plate 42 (Figs. 71—73).

« 1, 2 Sections of livers of infected snails.

« 3 4 Sections of mesentery of infected guinea pig showing the flukes in the veins in longitudinal and transversal cut.

« 5 Liversection from guinea pig including a transversal cut of female *Sch. M.*

The figures show photographs taken from stained preparations by J. PINTO, photographer of the institute.

Plate 43 (Figs. 1—4).

Fig. 1 a–d Adult specimen of *Planorbis olivaceus*. Shell in dorsal and ventral aspect, in profil and in transverse section; f adult specimen with upper half of shell removed, exposing the animal (combined drawing), e section of a small and aberrant specimen. Nat. size.

« 2 Shell of adult *Planorbis guadeloupensis*, a dorsal, d ventral aspect, b transversal section, c natural size.

« 3 The same refering to *Pl. centimemetralis*.

« 4 The same refering to *Planorbis Boissyi*.

In the plate the sections in horizontal position show the mouth to the right. If we consider the shell sinistral, the ventral side was turned upwards and the dorsal downwards. The section in vertical position show the mouth below.