

THE AMERICAN JOURNAL OF HYGIENE

VOL. 1

JANUARY 1, 1921

No. 1

THE DEVELOPMENT OF THE JAPANESE BLOOD-FLUKE, *SCHISTOSOMA JAPONICUM* KATSURADA, IN ITS FINAL HOST.*

BY WILLIAM W. CORT, Ph.D.,
Associate Professor of Helminthology,
School of Hygiene and Public Health,
Johns Hopkins University.

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(Received for publication October 1st, 1920.)

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I. COMPARISON OF THE CERCARIA OF *Schistosoma japonicum* WITH THE ADULT.

Since the discovery of the intermediate host of *Schistosoma japonicum* by Miyairi and Suzuki in 1913, our knowledge of the life-

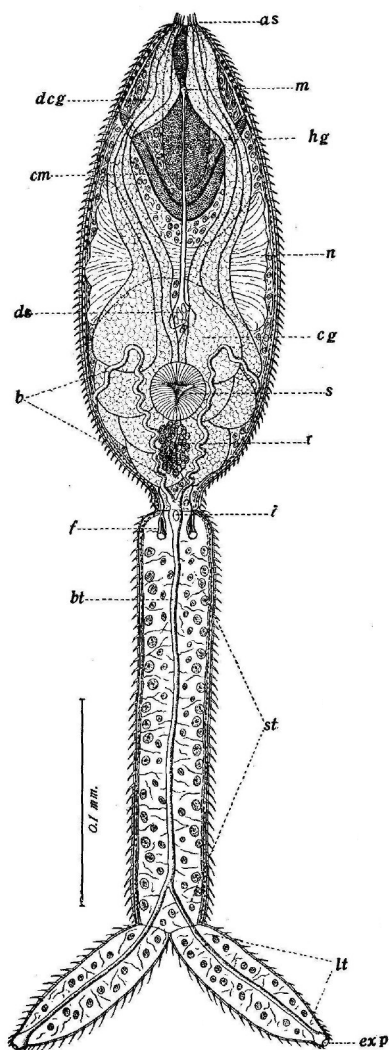
* A. contribution from the Department of Medical Zoölogy of the School of Hygiene and Public Health of the Johns Hopkins University.

cycle of the human blood-flukes has been very greatly increased. Very little is known, however, of the development after the cercaria enters the final host. The studies recorded in this paper were undertaken with the hope of filling in, to some extent, this gap in our knowledge in the case of *Schistosoma japonicum*. In order to point out the problems involved in this investigation, I will make a brief comparison between the cercaria of this species and the adult.

The cercaria of *S. japonicum* (Text Figs. 1 and 2) * is very highly specialized for that critical period of intense activity from the time that it leaves the shelter of its snail intermediate host until it has penetrated safely through the skin of its final mammalian host.

During this period two demands are made upon the activities of the cercaria. One of these is for locomotion, both freely in the water and on a surface. For this activity the cercaria has a well developed muscular system, a strong tail, a ventral sucker which can be firmly attached, and a method by which it can take hold with its anterior end. Details of the methods of locomotion of the cercaria of *S. japonicum* have been reported in a previous paper (Cort, 1919, 502-505). The second demand that the cercaria must be prepared to meet is that of penetration through the thick skin of the mammalian host. The whole structure and activity of the cercaria is modified profoundly for this activity (Cort, 1919, 496-502). In fact, it has become essentially a mechanism for skin penetration. There have been developed very large cephalic glands (Text Figs. 1 and 2, *cg*) for dissolving tissue. The musculature of the body, and especially of the oral suckers, is definitely adapted for penetration, and the arrangement of the spines is an admirable adaptation for this purpose. This unusual development of the adaptive larval characters, especially the enormous size of the cephalic glands, has kept in a very undeveloped condition the primordial adult characters. The extreme immaturity of the cercaria is indicated by its small size, the slight development of its postacetabular region and the very rudimentary character of its nervous, excretory, digestive and reproductive systems

* In my paper on the cercaria of *S. japonicum* (Cort, 1919, 501) I described and figured forward pointing spines around the openings of the cephalic glands, which I believed aided the cercaria in penetration. Faust (1919, 168, Figs. 4 and 5) demonstrated in the cercaria of *S. mansoni* and related forms, that these spines on the anterior end of schistosome cercariae are hollow in the center, cap the openings of the cephalic glands, and that the secretions of these glands pour through the hollow spines. I have been able to confirm Faust's observations on the cercaria of *S. japonicum*.



TEXT FIG. 1. Cercaria of *S. Japonicum*, ventral view; *as*, anterior spines; *b*, excretory bladder; *bt*, excretory bladder of tail; *eg*, cephalic glands; *cm*, circular muscles; *dcg*, ducts of cephalic glands; *ds*, digestive system; *exp*, excretory pore; *f*, flame cell; *hg*, head gland; *i*, island in excretory bladder; *lt*, lobe of tail; *m*, mouth; *n*, nervous system; *st*, stem of tail; *s*, ventral sucker. (From Cort, 1919.)

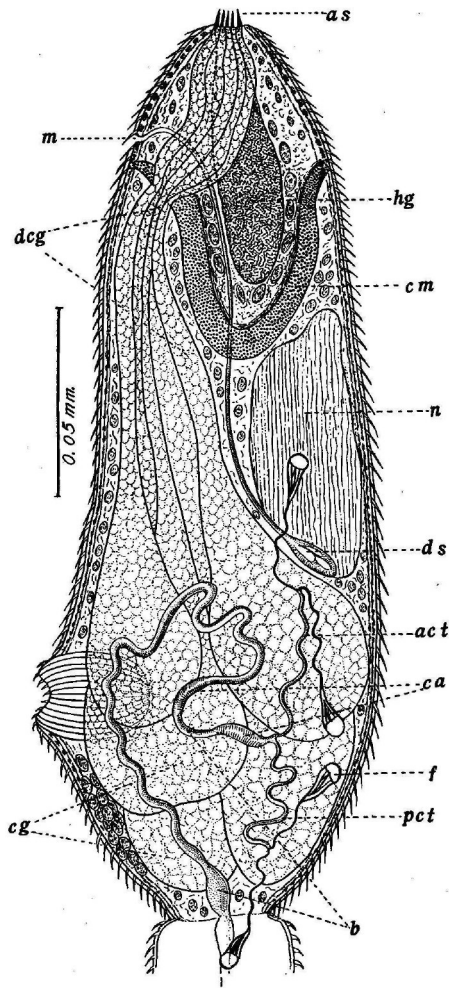
(Text Figs. 1 and 2). Finally, the sexual dimorphism which is such a striking characteristic of the adult has not been demonstrated in the cercaria.

The contrast in structure between the cercariae and the adults of *S. japonicum* (Figs. 11 (F) and 19 (M)) is so striking that practically no similarity whatever can be made out between the various organs, unless the intermediate stages in development are known. The structure of the adult of this species is dominated by sexual dimorphism and adaptations for reproduction. The shape of the male is fundamentally modified from the general distome condition by the development of the gynaeophoric canal for holding the female in copulation. The female, on the other hand, has a very elongate, narrow body. These modifications have come about chiefly by changes in the postacetabular region of the body which are correlated with the gradual development of the reproductive organs.

The morphological changes which are necessary to produce the adult of *S. japonicum* from the cercaria are truly remarkable. The highly developed adaptive larval characters are lost soon after penetration. The length of the body must be increased fifty to even over one hundred times. The nervous and excretory systems already functioning in the cercaria must be greatly extended to meet the requirements of this rapid increase in size. The digestive system which is not yet functional in the cercaria must be organized for its activities and greatly increased in length, to keep pace with the extending body. The whole complexity of the reproductive system must be gradually evolved from the small group of nuclei, which are the primordia of this system in the cercaria (Text Figs. 1, *r*), in some individuals becoming male organs and in others female. Finally, the development of the secondary sexual characteristics which differentiate the sexes early, and later produce extreme sexual dimorphism, goes hand in hand with the development of the reproductive systems.

II. MATERIAL AND TECHNIQUE.

The problems outlined above are interesting not only, because the changes from the cercaria to the adult in *Schistosoma japonicum* go on in the human body, but also from the more general biological viewpoint, since our knowledge is very inadequate of this stage in the development of the whole group of digenetic trematodes. An opportunity to attack this problem presented itself when on June



TEXT FIG. 2. Cercaria of *S. japonicum*, side view; letters, as in Text fig. 1; also *act*, anterior collecting tube; *ca*, ciliated areas; *pct*, posterior collecting tube. (From Cort, 1919.)

23, 1919, I received from Dr. Sadao Yoshida of the Osaka Medical College, a package containing a large number of dried specimens of *Blanfordia nosophora* (Robson), the intermediate host of *S. japonicum*. These snails had been collected on May 28 from an area where Japanese schistosomiasis is prevalent. About 85 per cent. of them became active when placed in water, and about 4 per cent. of the living snails were found to harbor the cercariae of *S. japonicum*.

During the evening of the same day on which this material was received, a tablespoonful of the dried snails was placed in each of three small glass aquaria in water, at a depth of about two and one half inches. On the following day, it was found that almost all of the snails had become active and that the water was swarming with cercariae.

At 4 P. M. of this day, June 24th, thirteen white mice were placed in the three aquaria. The depth of the water was such that they could rest their hind legs on the bottom and just keep their heads above the surface of the water. The mice were kept in the water about twenty-five minutes. The following morning, seventeen hours after the first exposure, the mice were again placed for about twenty minutes in water, containing the active cercariae from four infected snails which had been crushed.

The first of the mice was examined forty hours after the first exposure to infection, and three young worms were found in the blood. The other mice were examined on the tenth, twelfth, fourteenth, sixteenth, eighteenth, nineteenth and twenty-first days after the first exposure. In all these mice large numbers of the worms were found in the veins of the liver. In fact, the mice were so heavily infected that after the sixteenth day they began to die, and it was barely possible to keep the last one alive until after the twenty-first day. In addition to the material from these thirteen mice, there was also available for comparison a number of specimens taken from mice thirty days after infection.

To recover the young worms the livers of the mice were carefully teased apart in normal saline, and the worms picked out with a small pipette. In the earlier examinations it was necessary to search carefully with a microscope to find the young schistosomes. On the later days they had grown to such an extent that they could be seen with the naked eye. The worms were killed and fixed by pouring suddenly over them a hot saturated aqueous solution of corrosive sublimate containing 2 per cent. of acetic acid. This method proved

satisfactory since it caught the worms well extended. My observations were made from toto mounts prepared from this material.

The material available for study gave me a series of developmental stages from my smallest form, from the veins of the liver, 0.24 mm. in length, up to sexual maturity and copulation. A detailed study of that interesting period of reorganization from the cercaria to this smallest form will have to be left for future investigation. Since my studies were made on preserved material I have no data on the development of the excretory system. The present paper then includes a study of the changes in size and shape of the body, the changes in the suckers, the growth of the digestive system and the development of the reproductive organs and the secondary sexual characters which occurred in the veins of the livers of my experimental mice.

In addition to the data from my studies of the material discussed above, I shall include in this paper an account of all the phases in the life cycle from the free cercaria to maturity. This includes a discussion of the question of the time of determination of sex and possible sexual dimorphism in the cercaria, the method of penetration into the final host, the course of migration in the final host, and the early stages of development not included in my own studies. Most of the literature on these subjects is in the Japanese language. These publications were made available to me through the kind help of Dr. S. Yokogawa, of the Medical College of Formosa, and of Mr. Ibara, a graduate student in Johns Hopkins University who translated for me a part of Miyagawa's 1916 paper. I wish also to thank Miss Ethel Norris for her careful work in the preparation of the drawings included in this paper.

III. THE DETERMINATION OF SEX AND THE BEGINNING OF SEXUAL DIMORPHISM.

Since sexual dimorphism can be seen at a very early stage in the development of the larval schistosome in the final host, it seems perfectly evident that sexual differentiation is already present in the cercaria stage. From this consideration the question naturally arises whether there is not really present a sexual dimorphism in the cercaria stage. Altho many workers have made studies and measurements of the human schistosomes no one has reported such differences. I have myself, examined a number of cercariae of *S. japonicum* with this point especially in mind, without noting any dimorphism. Dr. S. Yokogawa

also informs me that he has made an extensive series of examinations and measurements of this cercaria in an attempt to find sexual differences, without success. Since the cercariae of the human schistosomes are very small and can extend and contract their bodies to an unusual extent, slight size differences might escape notice in the living specimens and be difficult, if not impossible, to detect in measurements of preserved material. Further, these studies have been made from cercariae obtained from infected snails which had been crushed to free the cercariae. Such material would contain various stages in the development. Therefore variations in size, due to differences in the developmental stages of the specimens studied, might obscure a slight sexual dimorphism. I believe that if careful measurements were made of large numbers of cercariae after their escape from the snails, it might be possible to demonstrate size dimorphism between the sexes of this species.

Recently, in some studies on a species of schistosome cercaria with eyespots, from *Planorbis trivolvis*, from Douglas Lake, Michigan, I have been able to demonstrate two distinct size types. This difference in size came to my attention first when I found that the curve plotted from the measurements of the cercariae which had escaped from a number of infested snails was distinctly bimodal. More extensive studies showed that the cercariae of this species fell into two distinct size groups. I further found from measurements of the cercariae from eleven infested snails that in the cercariae coming from a single snail only one of the size types was represented. The difference in size was so great between these two types that it could be recognized with the naked eye, when free swimming cercariae of the two types were placed in separate bottles. Measurements of the length of the body of the larger type showed a range of variation from 0.234 mm. to 0.28 mm., while in the smaller type, the range was from 0.207 mm. to 0.24 mm. Other measurements of the body and tail, which in this species is unusually large, showed like differences. The adult into which this cercaria develops is not known, although unsuccessful attempts were made to introduce it into ducks and rats. An analysis of its structure, however, places it near to the human schistosomes, in the family Schistosomidae. This relationship means that in all probability in the adult stage of this species the sexes are separate. I therefore, interpret the size differences in this species of cercaria as a sexual dimorphism. If this view is accepted, the fact that in one infested snail only one of the types of cercaria is repre-

sented, immediately becomes very significant. A more detailed account of the dimorphism of this species of cercaria will be published later in connection with a study of its structure and activities.

In this connection must also be cited the work of Tanabe (1919) on *Schistosoma japonicum*. This author found that in twenty-six out of thirty-one cases, when the cercariae from a single snail were used in infecting experimental animals, all the individuals developed were of the same sex. Dr. S. Yokogawa has given me permission to use in this connection, the results of some of his unpublished experiments along this line, which were performed several years ago. He found that when a cat, dog, or rabbit was infected with the cercariae from a single snail that worms of only one sex would develop. He also found that in these cases the worms would not develop to maturity. These two workers have developed independently the same hypothesis to explain the results of these experiments.

According to this hypothesis sex in the schistosomes is determined in the fertilized egg, and all the cercariae coming from a single miracidium are of the same sex. When all the individuals derived from the cercariae from a single snail were of the same sex, it would follow that the infestation in this snail was from a single miracidium or two or more miracidia of the same sex. In those cases where both sexes came from the same snail, this snail must have been originally infected with two or more miracidia representing both sexes. Now my findings recorded above in regard to dimorphism in a species of schistosome cercaria, and the presence in one snail of only one of these types lends further support to this hypothesis. Further, since in the life cycle of *S. japonicum*, the miracidium and the mother sporocyst are the only stages derived from a fertilized egg, it is in these stages that sex differentiation would theoretically be expected. Up to the present time, however, no one has examined these stages to determine whether they show a sexual dimorphism.

IV. PENETRATION OF THE CERCARIAE THROUGH THE SKIN OF THE FINAL HOST.

The structures of the body of the cercaria of *S. japonicum* which make possible the penetration through the thick skin of the mammalian host have been discussed above. It has also been clearly established (Fujinami and Nakamura, 1909; Katsurada and Hasegawa, 1910; Matsuura, 1909 and Fujinami, 1914) that infection with *S. japonicum* is produced by penetration of the cercariae through the

skin or mucous membrane. Infection by way of the digestive tract has been shown to be impossible (Tsuchiya, 1910; Fujinami and Nakamura, 1911; and Miyagawa, 1912a), since the cercariae cannot resist the action of the digestive juices. However, the infection with drinking water is possible, since the cercariae taken into the mouth may penetrate through the mucous membrane of the mouth and pharynx. Penetration through the skin of the cercaria of *S. japonicum* has been discussed most fully by Narabayashi (1914, 1916). He finds that the cercariae can penetrate through wet skin at any point where they become attached, although they actually seem to enter most frequently by way of the hair follicles. Usually, they entered singly, although sometimes two or three were found at the same place. In examinations of the skin from one to twenty hours after exposure to infection, the cercariae were found in the epidermis, dermis and subcuticula and sometimes in the deeper layers. The worms found in the skin tissues show various shapes and degrees of contraction. Usually, the tail is lost at the time of penetration through the skin, but in some cases it may be carried into the subcuticular layer. In one of my experimental mice I found a cercaria in the blood from the heart, with the tail still attached. The worms entering the skin seem to be attracted to the blood vessels, for soon numbers of them will be found in the capillaries, veins or lymph spaces of the dermis and subcuticula.

V. THE COURSE OF MIGRATION IN THE FINAL HOST.

The course which the larval blood flukes pursue in making their way from the skin to the blood vessels of the liver has been a matter of considerable controversy. Fujinami and Nakamura (1910) found the young parasites in the portal vein of a rabbit, three days after exposure to infection, and suggested that the course of migration in the body was probably by way of the blood stream. Miyagawa (1912; 1913; 1913a; 1913b) found the young flukes in the femoral and saphenous veins, in the hilus of the lymph glands, in the thoracic duct, and finally in the heart of experimental dogs. Later this same author (Miyagawa, 1916) also found the parasites in the capillary vessels of the lungs, kidney and intestinal walls, and in the left side of the heart. From his studies, he came to the conclusion that the young blood flukes might travel to the right side of the heart either by the veins or lymph vessels, be pumped into the lungs, pass the capillaries of the lungs and return to the heart. From the left side of the heart they would be carried into the systemic circulation, and

must again pass through capillaries to reach the mesenteric veins and the portal vein. Narabayashi (1914, 1916) agreed with Miyagawa that the above course is sometimes followed by the worms. He concluded, however, that the majority of the young blood flukes after reaching the lungs leave the blood vessels and migrate to the liver through the tissues. Strong evidence for this course has been furnished by the extended researches of Narabayashi (1916). This author infected large numbers of very young mice with the cercariae of *S. japonicum* and made serial sections of their whole bodies. He found that the majority of the cercariae, after passing through the skin, entered the veins and that only a few reached the heart by way of the lymph vessels, since most of those that got into the lymphatic system died in the lymph glands. He found them only rarely in the capillaries of the lungs, in the left heart and in the blood vessels of the kidneys. The larger number he found migrating through the connective tissue of the posterior mediastinum, along the large blood vessels and nerve trunks, while a smaller number was encountered also in the anterior mediastinum. Still others were found in the pleural cavity. He also found them in the tissues of the diaphragm and on the surface of the liver, but never in the hepatic, splenic and mesenteric arteries. Recently Suyeyasa (1919) repeated Narabayashi's experiments and came to the same conclusions. It seems probable, therefore, from these studies, that the usual course of migration is for the larval blood flukes to leave the blood vessels of the lungs, to pass through the diaphragm, and to enter the liver from its surface.

It is probable from the character of the migratory course described above that there would be considerable variation in the time necessary for the migration. It would be expected, therefore, that, in the course of a single infection larvae would keep entering the liver for a considerable length of time. That this actually happens is suggested by my finding very small larvae, less than 0.3 mm. in length, in the liver ten, twelve, and up to eighteen days after exposure to infection. This point will be discussed more in detail in a later section.

VI. THE MORPHOLOGICAL CHANGES IN THE DEVELOPMENT OF *S. japonicum* IN ITS FINAL HOST.

1. *Historical account.*

Up to the present time a detailed analysis of the morphological changes from the schistosome cercaria to the adult has not been made.

I find, however, that a number of authors have made observations on this stage of development. Most of these observations have been made on the development of *S. japonicum*, and most of them are included in papers written in Japanese. Leiper (1915) has figured a series of stages in the development of *S. haematobium* in its final host, but he does not describe or compare his stages, nor does he distinguish the sexes. Lutz (1919) in his discussion of *S. mansoni* gives very few data on this stage in development.

I will not attempt to discuss in detail all the observations which have been made on this stage in *S. japonicum*, but merely bring out the significant points in the studies of the various investigators. Miyagawa (1916) in his part of the Japanese monograph on *S. japonicum* (Fujinami, Tsuchiya and Miyagawa, 1916) discusses in some detail the work which has been done on this stage of development of *S. japonicum*. My discussion of the Japanese work is based upon reviews, upon a translation of the part of Miyagawa's paper dealing with this subject and upon discussions with Dr. S. Yokogawa.

Miyagawa (1916, 17) stated that in the larvae examined after entering the skin the "head gland" was found to be reduced in size, pressed to one side, and that later it disappeared. He also notes that in such worms the contents of the cephalic glands are much reduced in amount, and that these organs soon disappear.

No detailed morphological studies have been made of the development of the worms in the tissues, or during their migration to the liver. Miyagawa finds that the size of the young worms taken from the skin and the peripheral veins varies from 0.038 to 0.15 mm. in length, and from 0.012 to 0.068 mm. in width. Since the smaller limits of his ranges of variation are only a fraction of the size of the cercaria itself, it is evident that some of the specimens which he studied must have been extremely contracted, on account of the technique used in preservation. Narabayashi (1914) found young blood flukes in the skin having a length of 0.143 mm. and a width of 0.034 mm. Fujinami and Nakamura (1910) found a young fluke in the portal vein of a rabbit, three days after infection, with a length of 0.15 mm. and a width of 0.037 mm. Miyagawa (1916) also reports a worm in the portal vein of a dog, five days after exposure to infection, which measured 0.5 mm. in length and 0.058 mm. in width. Katsurada (1914, 372, Fig. 2) describes and figures a young stage 0.438 mm. in length and 0.12 mm. in width, taken from the liver of a dog on the seventh day after infection. This figure is evidently of

a male of about the stage of my Fig. 3 (*M*). The oral sucker in this specimen had become definitely rounded off and the intestinal ceca are well developed, and distended with a dark brown material, altho not yet united. Miyagawa (1916) also notes that the spines in the young worms up to 0.3 mm. can be very clearly distinguished, but that it is very difficult to see the spines, even in the preacetabular region in a specimen 1 mm. in length. He further records that at the 0.3 mm. stage the oral sucker has changed from the peculiar condition of the cercaria to a well rounded muscular organ, with a good sized mouth cavity.

Miyagawa (1916) also gives some interesting information on the early development of the digestive system. He finds that in the larvae taken from the skin the digestive system is already functioning, since it can be seen clearly and is distended with dark staining material. In the early stages it appears like a distended bag which is connected with the oral sucker by the narrow esophagus. A little later, the intestinal ceca develop, and in forms 0.2 to 0.3 mm. in length, the shape is like a horse shoe. A little later the ceca unite, and the common portion reaches almost to the posterior end of the body. Miyagawa offers a very interesting observation on the relation of the liver to the development of the blood fluke. He differs from Narabayashi's (1916) position that the liver is simply a station in the course of migration of the worms, and believes that it is the natural location for the worms and that only in it can growth go on normally. Further, it is only when females deposit eggs that the copulating worms work their way out from the blood vessels of the liver to the mesenteric veins.

According to the Japanese workers the reproductive organs become differentiated late, but sexual dimorphism appears early. Fujinami and Nakamura (1911) were able to distinguish the sexes in specimens 0.5 to 0.7 mm. in length, which had developed in dogs. According to these authors, the body of the male becomes early broader than the female, especially in the region of the branching of the intestinal ceca. Also, the suckers are somewhat larger in the male than in the female. They further find that there is a distinct difference in the region where the intestinal ceca unite. In the male the region between the intestinal ceca, just in front of the point of union is a long narrow triangle, while in the female this region, where the ovary develops is even at an early stage wider. Miyagawa (1916) notes that the differentiation of the reproductive organs comes com-

paratively late, and that they can not be clearly distinguished until a length of about 1 mm. is reached. He finds copulating worms twenty days after infection.

2. Growth in size.

One of the most striking changes in the development of *S. japonicum* in its final host is the remarkable increase in size. In the published records the sizes given for the body of the cercariae vary from 0.09 mm. to 0.23 mm. These variations for the most part depend on whether the measurements were made from living or preserved specimens, on the state of contraction, and on the method of preservation used. Since the body of a well extended, preserved specimen measures about 0.15 mm., I will use this size for comparison of the cercaria with further stages of development. The largest size which I have seen recorded for the adult of *S. japonicum* was 26 mm. in length for the female, and 22.5 mm. for the male. These measurements were the maximum found by Tsuchiya for living specimens, taken from man, and by Katsurada (see Katsurada, 1914, 366) from living specimens 21 months old, taken from a dog. To attain this size an increase in length of about 130 times over the cercaria is necessary.

The growth of *S. japonicum* in the final host may be divided into three periods, i.e. (1) from the penetration of the cercaria until the young worm reaches the blood vessels of the liver, (2) from the time of reaching the liver until sexual maturity, and (3) from sexual maturity to maximum size.

There is but little increase in size in the young worm which has not yet reached the liver. The three specimens which I found in the blood of the first mouse, examined forty hours after infection, appeared somewhat shrunken from the loss of the secretions of the cephalic glands, but showed no increase in length over the free cercaria. One of these larvae was very remarkable in having the tail still attached to the body.

My smallest specimen from the livers of the mice was 0.22 mm. in length and 0.1 mm. in width. This specimen was recovered 12 days after infection. Specimens almost as small were recovered on the 10th day, the 14th day and the 18th day after infection (see Table I). It can be concluded from these results that there is but little increase in size until the worms reach the liver, since such specimens as have been found in passage to this organ are very small and the smallest forms found in the liver are but little larger than the cercariae.

Further, the finding of very small specimens in the liver, as late as 18 days after infection, might be explained by considering that such a form had been delayed in its passage to the liver, and that favorable conditions for growth in size are not found until this organ is reached.

During the second period there is by far the most rapid increase in size. As in other trematodes, *S. japonicum* reaches sexual maturity long before the maximum size is reached. My earliest record

TABLE I.
Range of size in specimens found on different days.

	Number of days after first exposure to infection.						
	12	14	16	18	19	21	30
Male—							
Number of specimens measured*	10	8	9	7	13	13	10
Smallest	0.22	0.54	0.28	0.22	0.40	0.50	2.21
Largest	0.79	0.97	2.02	2.34	3.8	5.3	8.8
Female—							
Number of specimens measured*	12	15	10	13	10	10	10
Smallest	0.22	0.27	0.50	0.63	0.53	0.64	3.87
Largest	0.77	0.99	1.94	1.89	2.65	4.2	8.27

of copulation was nineteen days after infection. Individuals in copulation might be considered sexually mature, altho in the youngest pairs the uterus of the female did not yet contain eggs. The male in the youngest copulating pair which I measured, twenty-one days after infection, [Fig. 10 (F.) and 17 (M.)] had a length of 5.6 mm. and the female of 4.2 mm. It is interesting to note that in this early stage of copulation the female is considerably shorter than the male, while later the size relation is reversed. From these figures it can be seen that in the period of development in the liver of the mouse, up to sexual maturity, there can be an increase in less than twenty days from about 0.2 mm. to 0.3 mm. up to 5.6 mm. in the male, and 4.2 in the female, or an increase in length of 28 times and 21 times respectively. A comparison of the largest individual found on each of the days on which examinations were made indicates approximately the rate of growth during this period (see Table I). The largest individual, twelve days after infection, was 0.79 mm. in length, which is about five times the length of the cercaria, and about three

* This does not represent the total number of specimens examined, since only those which were apparently near the upper or lower range were measured for this table.

times the length of the youngest form which I have found in the liver. From the twelfth to the nineteenth or twenty-first days, when copulation takes place, the increase in size is still more rapid. In these seven to nine days the largest individuals show a gain in length of from five to seven times. It is during this period that the increase in size is most striking, since the worms which are barely visible to the naked eye in the earlier stages, on the later days are easily seen and picked out. In fact, the growth was so rapid that it could be noted with the naked eye at the two day periods. It is also during this period that in my heavily infected mice the worms clogged the blood vessels of the liver, and seriously affected their hosts.

The third period of growth of *S. japonicum* in its final host extends from sexual maturity until maximum size is attained. During this period, the growth is slow and extends over a long period of time. We have no very exact information in regard to the actual rate of growth during this period or how long growth may continue. In my experimental mice, from the 21st to the 30th day, the growth in size was much less than in the corresponding time in the second period (Table I). My experiments give me no further data in regard to growth during this period. Katsurada (1914) records specimens in mice which reached the size of 8 mm. in the male and 11 mm. in the female, 62 days after infection.

Further data on growth during the final period of development may be obtained from Tables II and III which I have copied from Katsurada (1914, 365 and 366). The data included in these two tables give some idea of the rate of growth during the third period, and the length of time that growth continues.

The records of the specimens taken from the dogs 82 days, 10 months and 21 months after infection, are especially to the point. Full size seems to have been attained in 21 months, since the largest specimen at this time is as large as the largest individuals ever recorded.

Katsurada (1914, 365) comes to the following conclusion in regard to the size-relation in *S. japonicum*.

Die Grösse der Tiere hängt von mancherlei Umständen ab, z. B. von ihren Entwicklungsstadien, von ihrer Individualität, von der Art des Wirtes und von sonstigen Verhältnissen. Nach unserer Beobachtung kann ein kleines Tierchen, dessen Körperlänge noch nicht ganz 5 mm. beträgt, schon reif sein.

His contention that the size of the host influences profoundly the size of the parasite is very interesting.

TABLE II.
Tabelle über Körperlänge des Schistosomum japonicum.

Autoren.....	Kasurada (1904).		Tschjira (1909).		Fujisami (1907).		Kasurada (1909).		Kasurada (1911).		Kasurada (1913).	
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Gesamtheit.....												
Durchschnittl. Körperlänge (mm.).....	10.43		16.1	21.3	16.0	17.8	10.92	14.5	8.0	11.0	12.8	10.6
Größter Längendurchmesser (mm.).....	12.0	12.0	19.5	26.0	21.0	23.0	13.0	17.0			15.0	12.0
Kleinstes Längendurchmesser (mm.).....	7.0	8.0	9.5	16.0	8.0	12.0	9.0	11.0			11.0	8.5
Zahl der Würmer.....	8		19	8			13	4			5	5
Zustand der Würmer.....	Formalinfixation		Frisch (aber 24 Std. n. d. Tod des Wirtes)				Formalinfixation		Frisch		Spiritusfixation	
Wirt.....	Katze		Mensch		Rind		Hund, gestorben, 82 Tage n. d. Ansteckungsversuch		Maus, getötet, 62 Tage n. d. Ansteckungsversuch		Hund, getötet, 10 Monate n. d. Ansteckungsversuch	

An important point which requires further discussion is the range of variation of individuals recovered on any given day after infection (see Table I). While this variation is very clear as early as the 12th day, with a maximum size of 0.79 mm. and a minimum of 0.22 mm., it is most strikingly exhibited during the later periods. On the 16th to the 19th days numbers of young distomes were found below 0.72 mm. in length, while the maximum on the 19th day had run up to 3.8 mm. in the male and 2.65 mm. in the female. Especially interesting was the finding of a male individual on the 18th day only 0.22 mm. in length. This specimen was very much contracted and probably represents about the stage of Fig. 2 (M.). By the 21st day no very small individuals were found, altho the range of variation was still quite great. By the 30th day the smallest individual found in a large series of examinations was a male, 2.21 mm. in length.

Since the mice were infected twice, with a lapse of about 17 hours between exposures, a slight degree of variation could be attributed to this cause. This cause is, of course, entirely inadequate to explain the great variations noted in Table I on all the days on which examinations were made, and especially the finding of very small individuals as late as 18 days after exposure to infection. To adequately explain these variations two things must be postulated, i.e., first a variation in the time taken for the passage from the skin to the veins of the liver, and second, the necessity of any given individual reaching the liver before there can be much increase in size. From the description given above, of the course of migration of the larval blood flukes, it seems certain that there must be a considerable variation in the time which is taken by the parasites in reaching their destination. From the large numbers which were found in the livers of the mice by the 12th day it seems probable that most of the larvae complete their course by this time. The view that only in the blood vessels of the liver can the young schistosomes find conditions favorable for their growth, is supported by the fact that the worms which have been found outside the liver in experimental animals, had increased but little in size over the cercaria. It is my opinion, therefore, that the range in size of the individuals found in the livers of my experimental mice was due to differences in the time taken in reaching the liver, and that the small individuals found in the later periods after infection, represented forms which had been considerably delayed in their way to the liver. That there is a definite

limit to the time which may be taken in making this course, is indicated by the fact that on the 30th day no small worms were found. Apparently all the worms, that were going to reach the liver had already arrived.

3. *Changes in shape.*

Probably the most remarkable of the changes in the development of *S. japonicum* in its final host are the changes in shape. In the cercaria (Text Fig. 1) unless in an extreme state of extension the length of the body is about three times its width. The length of the post-acetabular region is only about one-half that of the pre-acetabular, and the cross-section is round. The shape is but slightly different in my smallest specimen from the liver [Fig. 1 (F.) or (M.)], in which the length is about two and one half times the width. The length of the post-acetabular region is still less than the pre-acetabular and the cross-section is oval. Since the shape of the adult males and females [Figs. 11 (F.) and 18 (M.)] are so remarkably modified by the sexual dimorphism, the study of the changes by which these peculiarities are attained through a series of developmental stages is interesting and significant. The shape of the adults is so strikingly different from that of the cercaria that it is very remarkable that such changes could be accomplished in the short period of 18 or 19 days which it takes the developing fluke to assume the characteristic shape of the adult. These changes consist in a very great increase of the length in ratio to the width, an enormous increase of the post-acetabular region of the body, as compared with the pre-acetabular, and a gradual assumption of the secondary sexual characteristics which produce the sexual dimorphism of the adult. Since the changes in shape are very different in the male and the female, the sexes will be discussed separately.

The ratio of length to width increases very greatly in the female (Table IV) as can be seen by a comparison of figures 3 (F.), 5 (F.), 7 (F.), 8 (F.) and 10 (F.). In these forms, the ratios of length to width are as follows: 3 (F.) = 33:10; 5 (F.) = 20.3; 7 (F.) = 12:1; 8 (F.) = 18:1; 10 (F.) = 28:1.

In the specimens, 30 days old, from my experimental mice this ratio varied from 50:1 to 90:1. The width in all these ratios was measured in the region of the ventral sucker. After the reproductive organs are fully developed, the post-ovarian region becomes considerably wider than the pre-ovarian. This is shown in Fig. 11 (F.),

and Katsurada's measurements (see Table III) of three 21-month-old females, in copula, in which the ratio of length to width of the pre-ovarian region is about 200:1, while that in the post-ovarian region is only about 50:1.

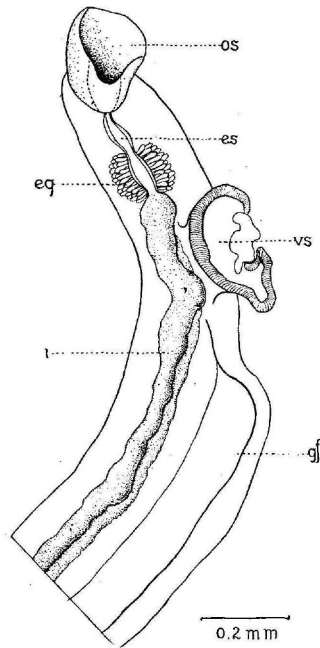
The great increase in length of the female occurs almost entirely in the post-acetabular region and is correlated with the development of the reproductive organs and the extreme attenuation of the body. In my smallest form which can surely be considered a female [Fig. 2 (F.)], the growth of the post-acetabular region has already brought the acetabulum in front of the middle of the body, and the pre-acetabular region is 48 per cent. of the total body length. In a series of females the percentage of the total body length occupied by the pre-acetabular region decreases rapidly with growth, as follows: Fig. 3 (F.) = 43 per cent.; Fig. 4 (F.) = 37.5 per cent.; Fig. 5 (F.) = 11 per cent.; Fig. 10 (F.) = 6 per cent. In the females of the thirty-day period this percentage has been reduced as low as 3 to 4 per cent. The pre-acetabular region also becomes distinctly narrower with growth.

Another change in the shape of the body of the female is an increase in thickness which changes the shape of the cross-section from an oval, in the early stages, to a circle in the later stages. This modification is completed at about the size of 7 (F.). When the body has become rounded in cross-section the young female worm comes to lie on the side and tends to curl up [See Figs. 8 (F.) and 9 (F.)].

In the males of *S. japonicum* the changes in shape are of an entirely different character from those in the female. In the male the length increases very much in ratio to the width, but not to the extent noted above, for the female. The changes in the ratio of the length to the width up to the time of the formation of the gynaeophoric canal are illustrated by the following series, i.e., Fig. 2 (M.) = 30:11; Fig. 4 (M.) = 44:13; Fig. 7 (M.) = 5:1; Fig. 9 (M.) = 6:1. After the formation of the gynaeophoric canal this change in ratio is even more rapid, as is shown by the following series: Fig. 11 (M.) = 7:1; Fig. 14 (M.) = 9:1; Fig. 17 (M.) = 16:1.

Also the increase in length of the post-acetabular region is not quite as great, as in the female. In a typical male series, the percentage of body length which is occupied by the pre-acetabular region, is as follows: Fig. 5 (M.) = 40 per cent.; Fig. 7 (M.) = 31 per cent.; Fig. 10 (M.) = 22 per cent.; Fig. 14 (M.) = 21 per cent. As development proceeds, the pre-acetabular region becomes dis-

tinctly set off from the rest of the body (Fig. 10 (M.) and Text fig. 3), and becomes round in cross section, not sharing in the flattening of the post-acetabular region, in connection with the formation of the gynaecephoric canal.



TEXT FIG. 3. Anterior region of half-grown male specimen of *S. japonicum*, to show an early stage in the development of the gynaecephoric canal; *eg*, esophageal gland; *es*, esophagus; *gf*, fold of gynaecephoric canal; *i*, intestine; *os*, oral sucker; *vs*, ventral sucker.

As noted above, from an early stage in development, the post-acetabular region of the male is distinctly wider than in the female. Also, the body in this region tends to become thinner [Fig. 4 (M.), 5 (M.), 10 (M.)]. In the earlier stages the post-acetabular region

is not set off from the rest of the body. It is only when the length of the young distome approaches 2 mm. that the characteristic shape of the post-acetabular region begins to be assumed. At this stage the post-acetabular region is set off distinctly from the pre-acetabular, the widening coming just behind the base of the acetabulum, which at this stage juts out considerably from the body.

Just after this stage, the sides of the thin post-acetabular region begins to grow up to form a trough [Figs. 11 (M.), 13 (M.), 14 (M.) and Text fig. 3]. As soon as this growth comes about, the shape of the male becomes such that it tends to turn over on its side and often to curve toward the dorsal side [Fig. 13 (M.)]. Soon the folding over becomes so great that the opening of the groove is almost closed by the sides of the body [Fig. 14 (M.)]. At this stage, the canal is almost completely formed, and is soon ready to enclose the female. During the course of this development, the body has become very thin.

4. *Development of the ventral sucker or acetabulum.*

In my description of the cercaria of *S. japonicum*, the following statement is made in regard to the ventral sucker (Cort, 1919, 494). "The ventral sucker is located at a point about three fourths of the distance from the anterior to the posterior end of the body. It is circular in ventral view with a depth considerably greater than its diameter. In the living animal the ventral sucker can be protruded so that it has almost the appearance of a proboscis. The sucker functions strongly in locomotion and is able to hold the cercaria against considerable pressure." As shown in Text fig. 1 the ventral sucker of the cercaria has only about one fourth the length of the oral sucker and one third its width. It has a diameter varying from about 0.018 mm. to 0.022 mm. Contrast with this the large size of the ventral sucker of the adults, especially the males, or even of the copulating pairs [Fig. 10 (F.) and 17 (M.)]. Katsurada (1914, 366) gives measurements of the ventral suckers of specimens taken from a dog 21 months after infection (See Table III). In this material the diameter of the ventral sucker varies, in the male from 0.5 mm. to almost 0.63 mm., and in the female from 0.091 to 0.114. This difference in the size of the ventral sucker of the male and female is apparent at a very early stage, and is one of the ways in which the sexes can be distinguished in the young worms [cf. Figs. 4 (F.) and 4 (M.)]. The stages in the development of the ventral sucker can be followed step by step in the females, and the increases

in size at the various stages seen in Table IV. The change in position of the ventral sucker, due to the relatively great increase in length of the post-acetabular region has been discussed in another connection.

In my youngest form [Fig. 1 (M. or F.)], in which I am not sure of the sex, the ventral sucker has almost doubled in size over the cercaria, having a length of 0.034 mm. and a width of 0.038 mm. In Fig. 4 (F.) in which the length of the body is almost twice that of Fig. 1 (F. or M.) the ventral sucker has a length of 0.067 mm. and a width of 0.068 mm. Beyond this stage, the increase in size of the ventral sucker of the female is more gradual, and not in proportion to the increase in body length. This can be seen by comparing Fig. 4 (F.) with Fig. 8 (F.), in which the length of the body has been almost quadrupled with only a 50 per cent. increase in the size of the ventral sucker (See Table IV). Beyond this stage, there is very little further increase in the size of the ventral sucker, although the length of the body increases very greatly. This is shown by a comparison of 8 (F.), with a total length of 1.8 mm., and a ventral sucker with a diameter of 0.099 mm., and the female from Katsurada's first copulating pair (see Table III), in which the length of the body was 23 mm., and the diameter of the ventral sucker only 0.114 mm.

In the early stages of the development of *S. japonicum* in its final host the ventral sucker is like that of any young distome. As the female elongates, so that the ventral sucker comes to lie in the anterior third of the body, it becomes thinner and begins to be distinctly set out from the surface of the body [Figs. 6 (F.)]. At the stage shown in Fig 7 (F.) the ventral sucker is saucer-shaped and somewhat pedunculate, and by the time the female becomes circular in cross-section, it assumes the characteristic adult shape of a shallow saucer set on a short stalk [Fig. 8 (F.)].

In the male the great increase in the size of the ventral sucker can be seen from my series of figures [Figs. 2 (M.) to 17 (M.)], and by comparing the measurements in Table IV. Here, as in the female, the rate of increase in size is greater in the earlier stage of development, but continues until growth is completed. Therefore, in comparing Fig. 3 (M.) with Fig. 4 (M.) (See also Table IV) it will be noted that while the increase in length is only about 50 per cent., the size of the ventral sucker has been doubled, while in the growth from the stage of Fig. 4 (M.) to that of Fig. 7 (M.) the length has been almost doubled, while the increase in size of the ventral sucker has been less than 50 per cent. A still further slowing of the rate of

growth is apparent from a comparison of Fig. 7 (M.) with Fig. 14 (M.) in which the length has been almost quadrupled, while the size of the ventral suckers has been only a little more than doubled (see also Table IV). This rate of increase becomes still less in the later stages. This can be clearly shown by a comparison of Fig. 14 (M.) with the adult male [Fig. 18 (M.)].

In the male the change in shape of the ventral sucker, during development, is even greater than in the female. At early stages in the male, the ventral sucker becomes very thin and flexible, as is shown by the irregularity of its shape, and it juts out from the body [Figs. 4 (M.) and 5 (M.)]. At an early stage in the formation of the gynaeophoric canal the ventral sucker has assumed the characteristic shape of the adult [Fig. 11 (M.) and Fig. 14 (M.)]. The ventral sucker is very thin and flexible, with the outline quite irregular and varying from saucer shape to cup shape. It is always set off from the body with a distinct stalk, and after the formation of the gynaeophoric canal it is set in the hollow formed between the rounded neck region and the anterior limits of the sides of the gynaeophoric canal (Text fig. 3).

There is, of course, a considerable degree of variation in the size of the ventral sucker in individuals of the same length. This variation, however, is not sufficient to invalidate the course of development as outlined above.

3. Development of the oral sucker.

The oral sucker of the cercaria of *S. japonicum* has been described in an earlier paper (Cort, 1919, 496 to 497), and is shown in Text figs. 1 and 2. The oral sucker at this stage has scarcely any of the permanent characteristics of the adult, and its structure is very much modified by the presence of adaptive larval characters, and by its relation to the activities of the cercaria in locomotion and penetration. The oral sucker of the cercaria occupies almost one-third of the body length, and the mouth and buccal cavity are very small (Text figs. 1 and 2, M.). The oral sucker of the adult [Figs. 11 (F.) and 18 (M.)] is entirely different from that of the cercaria. While it has increased very greatly in size, it has come to occupy only a very small fraction of the body length. The oral sucker has now assumed the shape of a funnel with a very large mouth and thin lips. The buccal cavity is funnel-shaped and small at the point where it joins the esophagus. The mouth opens on the ventral side, and the shape of the sucker

and buccal cavity is asymmetrical. At the stages shown in Fig. 8 (F.) and Text fig. 3 the oral sucker has already assumed its characteristic adult condition. A comparison of these figures with the cercaria show how profoundly this structure has been modified in development.

In the smallest individual which I have figured [Fig. 1 (F. or M.)] the oral sucker has already changed fundamentally from the condition of the cercaria. The adaptive larval characters, i.e., the anterior spines, the ducts of the cephalic glands and the "head gland" have already disappeared. The mouth and buccal cavity have increased in size, the latter being already funnel-shaped. The characteristic ventral position of the mouth is apparent at this stage, establishing definitely its relation to the mouth, as shown in the cercaria [Text fig. 1 (M.)]. While the diameter of the mouth at this stage is greatly increased over the condition of the cercaria, it is as yet only a little over one fourth the diameter of the oral sucker. The oral sucker in this specimen occupies slightly over one fourth of the body length, the length of the body in this specimen being 0.24 mm., and the length of the oral sucker 0.063 mm. The oral sucker at even this early stage is much more definitely set off from the rest of the body than in the cercaria, and its muscles are developed in relation to the sucking activity of the mouth and buccal cavity.

Early in the development there is a greater proportional increase in size in the oral sucker of the male than of the female. In fact, the easiest way to distinguish the sexes in the earlier stages is by a comparison of the size of the oral suckers. This difference is shown clearly by comparing the increases in size of the oral sucker in relation to the increases in length of the body of a series of females [Figs. 2 (F.), 3 (F.), 4 (F.), 5 (F.), 7 (F.) and 8 (F.)], with a comparable series of developmental stages of males [Figs. 3 (M.), 4 (M.), 7 (M.), 9 (M.), 10 (M.), 14 (M.)] (see also Table IV). In this series of females the body length increases from 0.27 mm. to 1.85 mm., while the diameter of the oral sucker only increases from 0.05 to 0.092 mm. On the other hand, in the series of males the body length increases from 0.3 mm. to 3.1 mm., and the diameter of the oral sucker from 0.074 mm. to 0.227 mm. Katsurada records in fully developed males (Table III) measurements of the oral sucker ranging from 0.456 mm. to 0.604 mm. There is very little, if any, increase in size in the oral sucker of the female beyond the stage of 8 F.

The ratio in size of the oral sucker and the ventral sucker shows

an interesting fluctuation in the course of the development, both of the male and the female. In the cercaria the oral sucker is between three and four times the size of the ventral sucker. At the stage in development, represented by Figs. 4 (F.) and 4 (M.) the suckers are very nearly equal in size. From this time on (see Table IV), the ratio is reversed, and the ventral sucker is constantly larger than the oral sucker.

The most striking change in the development of the oral sucker is the increase in the size of the mouth and buccal cavity. Even at the stage of Fig. 1 (F. or M.) the width of the mouth has already increased greatly beyond the condition in the cercaria (Text figs. 1 and 2), and the buccal cavity is beginning to assume the characteristic funnel shape. As development proceeds, the mouth increases rapidly in size [cf. Figs. 2 (M.), 3 (M.), 4 (M.), or Figs. 2 (F.), 3 (F.), 4 (F.)], coming to occupy most of the ventral surface of the oral sucker. The buccal cavity soon assumes the condition approximating the adult [Text fig. 3 and Fig. 8 (F.)]. It can be seen, by comparing the oral suckers at the stages of these figures with the condition in the cercaria (Text fig. 2), that the asymmetrical condition of the oral sucker which is apparent in the cercaria persists in later stages. In Text fig. 3, for example, it can be seen that the distance from the anterior lip of the oral sucker to the passage into the esophagus is longer than the distance from the posterior lip to this point, and that consequently the same relation is true in the buccal cavity.

6. Changes in the digestive system.

The digestive system in the cercaria of *S. japonicum* (Text figs. 1 and 2) is not functional, and is in a very rudimentary stage of development. This is especially indicated by the fact that the intestinal region, which attains such an extensive development in the adult [Figs. 11 (F.) and 18 (M.)], is represented in the cercaria only by a heart-shaped sac (Text fig. 1, *ds*). The remarkable changes which this system must pass through to attain the adult condition may be divided into three periods, i.e., (1) from the condition in the cercaria to the beginning of functional activity, (2) from the beginning of functional activity to the union of the intestinal ceca, (3) from the union of the ceca until completion of development. Of the first period, we know but little, altho Miyagawa's (1916) account of the development of this system indicates that functional activity is attained very soon after penetration (see literature section). The sec-

ond period is characterized by the growth of the intestinal ceca. During this period, as indicated by Miyagawa's (1916) account and my own earlier stages, there is intense functional activity which is indicated by the very great distension of the intestine with food material [Figs. 3 (F.) and 3 (M.)]. The third period is characterized by a very rapid extension of the intestine, to keep pace with the growth of the body.

My earliest stage [Fig. 1 (M. or F.)] shows a great advance in the development of the digestive system over the cercaria, since the intestinal ceca are well developed and distended with brownish food material, indicating functional activity. There is, therefore, a big gap in my material, which includes the early stages of organization of the digestive system in preparation for functioning. Miyagawa's account (see section on literature) partly fills this gap. This organization must come very early, since the young worm needs an abundant supply of food, as soon as it has entered the final host, to prepare itself for the period of rapid growth. In my earliest stage [Fig. 1 (M. or F.)] the esophagus is well developed and already surrounded by the characteristic glandular area. This esophageal gland is made up of closely packed unicellular glands, which open separately into the esophagus. The only noticeable changes in the esophagus, as development proceeds, are increases in its diameter and length, corresponding to increases in size of the pre-acetabular region.

The development of the intestinal ceca up to the time of union is shown in Figs. 1 (M. or F.), 2 (M.), 2 (F.) and 3 (M.). These figures show an elongation of the intestinal ceca, corresponding to the increase of the post-acetabular region, and an approach of the ends of the ceca which fore-shadows their union. The most characteristic thing during this period is the great distension of the intestine with brownish food material, which makes its bulk very large in proportion to the size of the post-acetabular region of the body. The union of the intestinal ceca comes, when the developing worms have reached a length of about 0.3 mm. to 0.4 mm. [Figs. 3 (F.) and 4 (M.)]. For a considerable time after the union of the ceca there is still noticeable a considerable distension of the intestine with food material [Figs. 5 (F.), 5 (M.) and 7 (M.)]. As the length of the post-acetabular region of the body increases, and the intestine becomes longer, it is less distended with food material, and assumes more the narrow irregular appearance of the fully developed condition [Figs. 5 (F.), 7 (F.), 8 (M.) and 9 (M.)]. In the later stages of development the

intestine of the male becomes wider than that of the female. From cross-sections, however, it can be seen that this difference is compensated for, in the female, by a greater thickness of the intestine. These differences are of course, correlated with the differences in thickness of the body in the two sexes.

The relative length of the divided and the united regions of the intestine, at various stages, can be seen from Table IV. At the time of union of the intestinal ceca, two points are definitely established, i.e., (1) the point of bifurcation of the intestinal ceca which remains throughout all the further stages of development just in front of the base of the ventral sucker, and (2) the posterior tip of the intestine which remains always very close to the posterior tip of the body. As the body length increases, these two points remain constant and there is an increase in length of both the divided and the united portion of the intestine, to keep pace with the increase in the body length.

Soon after the union of the intestinal ceca a distinct sexual difference can be noted. In the adult female, the area just in front of the intestinal ceca is much wider than in the male, since it contains the ovary and other parts of the reproductive system. An examination of the figures of the early stages of the female [Figs. 3 (F.), 4 (F.), 5 (F.), 6 (F.)] shows that this area is already apparent at an early stage of development, and contrasts with the condition of this region in the male [Figs. 4 (M.), 7 (M.), 8 (M.)]. This difference is one of the points of sexual dimorphism which makes early discrimination of the sexes possible.

7. *Development of the reproductive organs.*

No attempt was made to trace the histogenesis of the reproductive organs. I will note, however, certain of the important stages in development. It is only late in development that the reproductive organs themselves become clearly differentiated. In the male it was difficult to make out the outlines of the reproductive organs in the early stages. In a male, 2.5 mm. in length, taken from a mouse nineteen days after infection, the outlines of the seminal vesicle and the testes were clear. The testes were almost round, and composed of dense nuclei, the spermatogonia, with considerable space between. The testes at this stage had an embryonic appearance, and there was no trace of spermatogenesis. The length of the total testes group of seven, was 0.175 mm., and the testes had a diameter ranging from 0.023 to 0.032 mm. The testes had distinct spaces between them. A

TABLE IV.
*Measurements of a series of development stages of Schistosoma japonicum in mm.**

Individual Characteristics.	1 (F. or M.).	2 (F.).	3 (F.).	4 (F.).	5 (F.).	6 (F.).	7 (F.).	8 (F.).	10 (F.).	11 (F.).	2 (M.).	3 (M.).
Length.....	0.24	0.27	0.325	0.48	0.81	0.91	1.1	1.85	4.2	8.2	0.3	0.3
Width at ventral sucker.....	0.1	0.1	0.1	0.125	0.12	0.11	0.1	—	—	0.1	0.11	0.115
Width at middle of pre-acetabular region.....	0.08	0.085	0.085	0.075	0.1	0.09	0.075	—	—	—	0.095	0.1
Width at middle of post-acetabular region.....	0.1	0.1	0.115	0.12	0.14	0.12	0.12	0.1	0.15	—	0.095	0.12
Length of pre-acetabular region.....	0.15	0.13	0.14	0.18	0.23	0.2	0.12	0.2	0.25	0.45	0.16	0.15
Percentage of total length taken up by pre-acetabular region.....	62.0	48.0	43.0	37.5	28.0	22.0	10.0	11.0	6.0	5.0	53.0	50.0
Ratio of length to width.....	—	—	33:10	—	20:3	—	12:1	18:1	28:1	30:11	—	—
Length of oral sucker.....	0.063	0.059	0.069	0.067	0.071	—	0.057	0.075	—	0.1	—	0.069
Width of oral sucker.....	0.055	0.05	0.05	0.063	0.084	—	0.092	—	—	—	—	0.074
Length of ventral sucker.....	0.034	0.042	0.053	0.067	0.067	—	0.067	0.099	—	0.1	—	0.035
Width of ventral sucker.....	0.038	0.039	0.061	0.068	0.084	—	0.097	—	—	—	—	0.039
Length of bifurcated part of intestine.....	0.101	0.126	0.153	0.168	0.378	—	0.609	—	—	—	—	0.161
Length of united part of intestine.....	—	—	—	0.042	0.095	—	0.174	—	—	—	—	—
Width of intestine.....	0.025	0.025	0.044	0.067	0.042	—	0.021	—	—	—	—	0.032

* The numbers given to the individuals in Table IV correspond to the numbers given to the figures in Plates I. to IV.

TABLE IV (continued).

Individual Characteristics.	4 (M.).	5 (M.).	7 (M.).	8 (M.).	9 (M.).	10 (M.).	11 (M.).	13 (M.).	14 (M.).	15 (M.).	17 (M.).	18 (M.).
Length.....	0.44	0.56	0.8	1.07	1.5	1.8	1.7	2.2	3.1	3.8	5.6	8.1
Width at ventral sucker.....	0.13	0.15	0.16	0.21	0.25	0.24	0.25	—	—	—	—	0.2
Width at middle of pre-acetabular region.....	0.11	0.12	0.12	0.16	0.22	0.18	—	—	—	—	—	—
Width at middle of post-acetabular region.....	0.14	0.15	0.14	0.19	0.22	0.28	—	—	—	—	—	—
Length of pre-acetabular region.....	0.21	0.26	0.25	0.34	0.47	0.4	0.5	0.5	0.65	0.6	0.85	0.7
Percentage of total length taken up by pre-acetabular region.....	47.0	40.0	31.0	32.0	31.0	22.0	28.0	23.0	21.0	18.0	18.0	9.0
Ratio of length to width.....	44:13	—	5:1	5:1	6:1	—	—	—	9:1	—	16:1	—
Length of oral sucker.....	0.088	—	0.105	—	0.202	0.168	0.197	—	0.179	0.252	—	0.3
Width of oral sucker.....	0.103	—	0.128	—	0.17	0.176	—	—	0.227	—	—	—
Length of ventral sucker.....	0.082	—	0.122	—	0.208	0.242	0.210	—	0.273	0.302	—	0.3
Width of ventral sucker.....	0.095	—	0.128	—	0.21	0.252	—	—	0.294	—	—	—
Length of bifurcated part of intestine.....	0.179	—	0.357	—	0.777	1.144	0.79	—	1.59	1.69	—	—
Length of united part of intestine.....	0.08	—	0.168	—	0.225	0.426	0.336	—	0.84	1.4	—	—
Width of intestine.....	0.042	—	0.057	—	0.021	0.063	—	—	—	—	—	—

more advanced stage in development was seen in a male, 3.7 mm. in length, taken from a mouse twenty-one days after infection. The testes in this form were denser and appeared to be in the process of spermatogenesis. This male was just a little smaller than the smallest male found in copulation. Probably, therefore, it represents the stage of the beginning of sexual maturity. The total length of the testes group in this form was 0.205 mm. The individual testes were compact bodies, somewhat rounded, but wider than long. The length of the individual testes was about 0.023 to 0.032 mm., and their width 0.042 to 0.048 mm. The anterior and posterior testes were almost round, and distinct spaces were visible between the individual testes.

The fully matured condition was represented by a male 8 mm. in length [Fig. 18 (M.)], taken from a mouse thirty days after infection. In this specimen the total length of the testes area was 0.532 mm. The dorso-ventral diameter of the middle five testes was greater than their length, while the anterior and posterior ones were practically spherical. The smallest testes in the group had a width of 0.095 mm. and a length of 0.067 mm., while the largest had a length of 0.076 mm. and a width of 0.105 mm. The diameter of the end ones was 0.095 mm. These testes were very compact, surrounded by a definite connective tissue sheath, and were in contact.

In males of about 1 to 2 mm., traces of the reproductive organs could be made out, but their outlines could not be clearly distinguished. In earlier stages I was unable, in the material studied, to find the *Anlage* of the male system.

In very early stages the *Anlage* of the ovary can be distinguished in the widened area in front of the place of union of the intestinal ceca. The smallest form in which I was able to distinguish any of the other organs was a specimen 1.44 mm. in length, taken from the liver of a mouse, eighteen days after exposure to infection. At this stage the ovary had a length of 0.095 mm. and a width of 0.030 mm. Just in front of the ovary the position of Mehlis' gland could be distinguished. The uterus was very clearly defined and could be traced, as a straight tube, in the region between the intestinal ceca, from just in front of Mehlis' gland to the genital pore. Parts of both the vitelline duct and oviduct could be distinguished, and the position of the vitellaria was indicated by denser areas in the posterior end of the body. At this early stage, therefore, all parts of the reproductive system are differentiated.

In another specimen, 3.2 mm. in length, which was much coiled,

the ovary had a length of 0.171 mm. and a width of 0.042 mm. The outlines of the lobes of the vitellaria could be clearly distinguished along each side of the body for the whole length of the post-ovarian region, but they did not have the characteristic brownish color which comes with functional activity. The outlines of the other organs were clearly defined. This form evidently represents a stage, just before sexual maturity was attained. In a fully matured specimen [Fig. 11 (F.)] the ovary had a length of 0.4 mm. and a width of 0.15 mm., the vitellaria were very dense, and had a brownish color. There were in this specimen about 50 eggs in the uterus.

VII. SUMMARY.

1. The contrast is very striking between the cercaria of *S. japonicum*, in which the structure of the body is greatly modified by adaptive larval characters for locomotion and penetration, and the adult in which the sexes are separate and there is an extreme sexual dimorphism.

2. Sexual dimorphism has never been demonstrated in the cercariae of the human schistosomes, although the finding of a size dimorphism in a closely related species of schistosome cercaria suggests that undetected differences may be present.

3. The finding by Japanese workers, that when an experimental host is infected with cercariae of *S. japonicum* from a single snail, all the resulting individuals are in the great majority of cases of the same sex, and my own findings that in the schistosome cercaria from Douglas Lake, in fifteen infected snails studied, all the cercariae from a single snail were of the same size type, suggests the theory that sex in the schistosomes is differentiated in the miracidium stage, and that all cercariae which develop from a single miracidium are of the same sex.

4. The work of Japanese investigators on the life history of *S. japonicum* has demonstrated that infection with this species is always by penetration of the cercaria through the skin or the oral or pharyngeal mucous membrane, and never by way of the digestive tract, and that the cercariae can penetrate easily at any point through wet skin, although the most frequently enter by way of the hair follicles.

5. The course by which the larval blood fluke reaches the blood vessels of the liver has been the subject of considerable controversy. Soon after exposure to infection, the larvae will be found in the epidermis, dermis and subcuticula, and later most of them enter the

small blood vessels and lymph spaces. They are carried to the heart, either by the venous system or by the lymph vessels, although the former seems to be the most frequent course, since most of those which get into the lymph system seem to die in the lymph glands. From the heart they are carried to the lungs. From the blood vessels of the lungs, two courses have been traced. The first course is through the capillaries of the lungs back to the heart, from the heart by the arterial system, and through the capillaries to the hepatic portal system. Those larvae which follow the second course which is probably by far the most frequent, leave the blood vessels in the lungs, penetrate through the lung tissue, enter the peritoneal cavity by way of the connective tissue of the posterior mediastinum and to a lesser extent of the anterior mediastinum, following with preference the course of the large blood vessels and nerve trunks and finally penetrate into the liver, where they enter the hepatic portal system.

6. Soon after penetration through the skin, the tail of the cercaria is lost and the cephalic and head glands degenerate. There is very little increase in size, until the larvae reach the liver, altho the digestive system becomes organized for functioning, and the oral sucker begins to assume its true character.

7. In the earliest stage found in the liver, it is impossible to distinguish the sexes, but at the stage between 0.3 mm. to 0.4 mm. the males show distinctly larger suckers, and a broader body than the females, and the females have a distinctly broader area in front of the union of the intestinal ceca, where the ovary later develops.

8. To attain the largest size recorded for this species the cercaria must increase in length over 100 times. The most rapid period of growth is from the time of reaching the liver to sexual maturity, when the worms may increase their length in less than 20 days by 20 to 30 times. Growth continues after sexual maturity, but is much slower.

9. The finding of larvae as small as 0.3 mm. in the liver, up to eighteen days after infection, can be explained by postulating that the worms grow but little in size, until they reach the liver, and that there is a variation in time for the migration course.

10. The increases in size are almost entirely in the post-acetabular region. As growth goes on, there is a very great increase in the ratio of length to width, which is much greater in the female than in the male. The body of the female soon becomes much narrower than in males of the same age, and becomes round in cross-section, while in the male the post-acetabular region gradually becomes flattened, and the sides grow up to form the gynaeceophoric canal.

11. The size of the suckers increases greatly in the course of development, but not in proportion to the increases in body size. In the male, this increase is much greater than in the female. In the cercaria the ventral sucker is only about one third of the diameter of the oral sucker. In an early stage of development, the suckers become about equal in size, and in later stages the ventral sucker is constantly larger than the oral sucker. The ventral sucker with increase in size becomes thinner, and juts out from the body, until in later stages it is saucer-shaped and has a distinct peduncle. The greatest change in the oral sucker is the great increase in the size of the mouth and buccal cavity.

12. From the very rudimentary condition of the cercaria the digestive system soon becomes horseshoe shaped, and very much distended with food material. The ends of the intestinal ceca unite at a stage of about 0.4 mm. in length. The divided and united portions both extend greatly, to keep pace with the increased length of the body. In the female the position of the point of union of the intestinal ceca and the greater width of the area in front of this point as compared with the male is influenced by the development here of the ovary.

13. Differentiation of the reproductive organs comes late. Although at an early stage, the *Anlage* of the ovary can be distinguished, it is not until the female attains a length of about 1.5 mm., that the outlines of the ducts and other organs can be clearly made out. In the male it was only in specimens over 2 mm. in length that the outlines of the testes could be clearly distinguished.

EXPLANATION OF PLATES.

All figures were drawn with a camera lucida and represent different stages in the development of *S. japonicum*, in experimentally infected mice. The numbers of the figures correspond to the numbers given to the individuals in Table IV.

Abbreviations used:

e, eggs; *eg*, esophageal gland; *es*, esophagus; *gf*, fold of gynaecophoric canal; *i*, intestine; *is*, intestinal space in female, where ovary develops; *n*, central nerve mass; *os*, oral sucker; *ov*, ovary; *tt*, testes; *vit*, vitellaria; *vs*, ventral sucker.

PLATE I.

FIG. 1 (F. or M.) Very immature specimen from liver of mouse, ten days after infection; length 0.24 mm., sex not certain, ventral view.

FIGS. 2 (F.), 3 (F.) AND 4 (F.). Very immature females from mouse's liver, twelve days after infection, ventral view.

FIGS. 2 (M.) AND 3 (M.). Very immature males from liver of mouse, twelve days after infection, ventral view.

FIG. 4 (M.). Very immature male from liver of mouse, sixteen days after infection, ventral view.

PLATE II.

FIGS. 5 (M.) AND 7 (M.). Immature males from liver of a mouse, fourteen days after infection, ventral view.

FIGS. 8 (M.) AND 9 (M.). Immature males from the liver of a mouse, sixteen days after infection, ventral view.

FIG. 5 (F.). Immature female from liver of a mouse, fourteen days after infection, ventral view.

FIG. 6 (F.). Immature female from liver of a mouse, sixteen days after infection, ventral view.

FIG. 7 (F.). Immature female from liver of a mouse, eighteen days after infection, ventral view.

FIG. 8 (F.). Immature female from liver of a mouse, nineteen days after infection, side view.

PLATE III.

FIG. 9 (F.). Immature female from liver of a mouse, nineteen days after infection, side view.

FIG. 10 (M.). Immature male from liver of a mouse, twenty-one days after infection, ventral view.

FIG. 11 (M.). Immature male from liver of a mouse, nineteen days after infection, side view.

FIG. 13 (M.). Immature male from liver of a mouse, eighteen days after infection, side view.

FIG. 14 (M.). Immature male from liver of a mouse, nineteen days after infection, ventral view.

FIGS. 17 (M.) AND 10 (F.). Male and female in copulation from liver of infected mouse, twenty-one days after infection.

PLATE IV.

FIG. 18 (M.). Sexually mature male from liver of mouse, thirty days after infection.

FIG. 11 (F.). Sexually mature female from liver of mouse, thirty days after infection.

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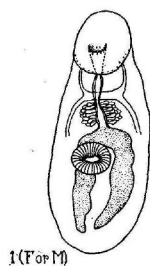
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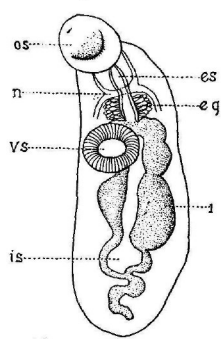
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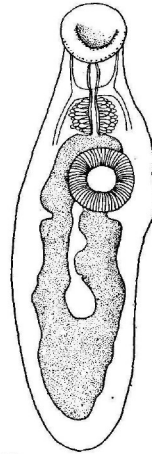
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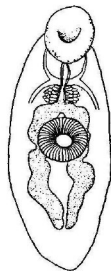
1 (F or M)



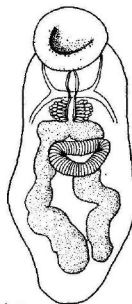
3 (F)



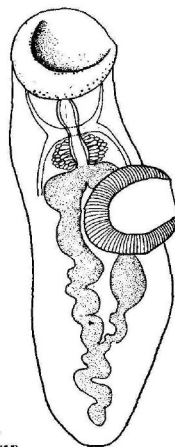
4 (F)



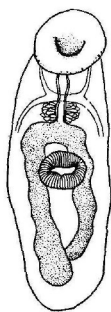
2 (F)



3 (M)



4 (M)



2 (M)

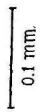


PLATE I.

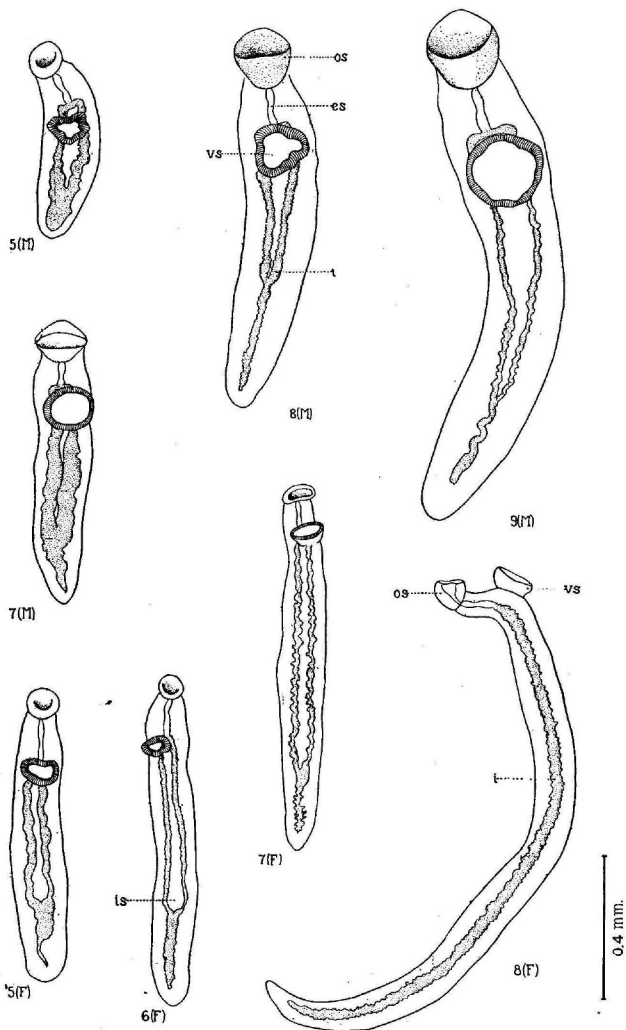


PLATE II.

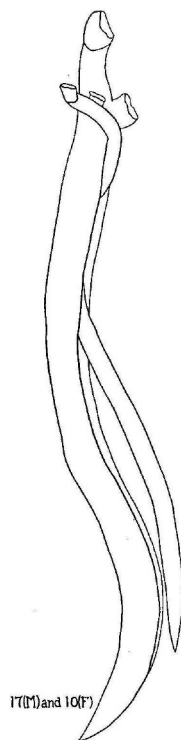
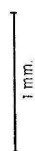
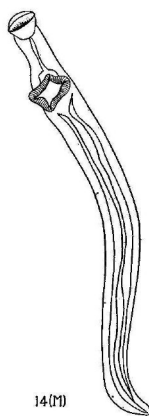
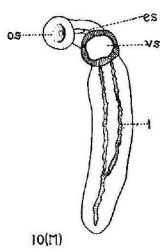
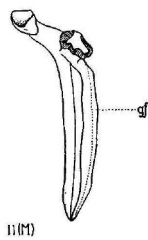
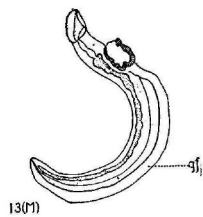
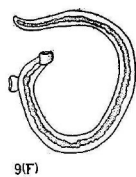


PLATE III.

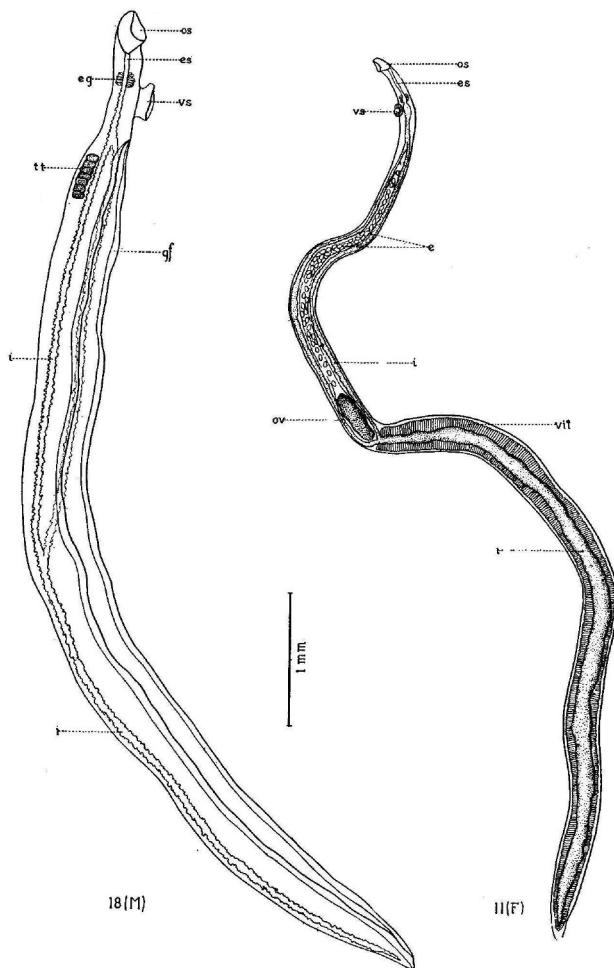


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