HUMAN PULMONARY DISTOMIASIS CAUSED BY PARAGONIMUS WESTERMANNI.

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PLATES 22 TO 31.

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INTRODUCTION.

Pulmonary distomiasis is caused by Paragonimus westermanni Kerbert, and prevails extensively in the Far East. Ringer (1) discovered the parasite in 1879 in a patient at Tamsui in Formosa, and it has since been found in various parts of Japan by several observers. In certain localities it prevails as an endemic disease, and has for a long time aroused the interest of Japanese investigators. The development of the worm has, however, remained unknown except for the fact that the eggs are ejected with the sputum and that they hatch in water into free miracidia.

Prevalence of Pulmonary Distomiasis in Formosa.

Although Ringer first found cases of pulmonary distomiasis in Formosa in 1879, the actual prevalence of the disease has remained unknown. In 1910 Nagano (2) reported that the disease prevailed in the northern part of Formosa around the Prefecture of Shinchiku. During 1913 and 1914 (3), I secured records of 1,249 cases, of which 922 occurred in the Prefecture of Shinchiku, the most thickly infected region on the island. I examined the pupils of all the public schools in the Prefecture of Shinchiku in December, 1914, and found that 4.3 per cent were suffering from the disease. The morbidity among the young is less than among adults. However, if we assume this percentage to be that of the whole population of the Prefecture of Shinchiku, there are 13,000 cases in this region alone. The results of my observation differ from those of
Matsuo and Yokokawa (4) regarding the morbidity in Sansaka, Koryo, Jukirin, and Nansho. The discrepancy is probably due to the fact that the people of those villages have sunk wells and stopped drinking the river water during the period between their investigation and mine. The infection is more prevalent among people living along large rivers, such as the Hozankei, Komodenkei, Chukokei, and Koryokei. The inhabitants of the mountainous regions also were thought to suffer from this disease, but no investigation had been undertaken. In 1914, appointed by the Commission of Investigation of Formosan Endemic Diseases, I went into the districts inhabited by savage tribes and found that in the lowlands an enormous number of cases, i.e., 50 per cent of the total population, was infected; in the highlands the cases seem to be less in number, although I was unable to carry out a thorough investigation there.


The Prefecture of Shinchiku and the villages of the savages in that vicinity are favorable districts for carrying out observations upon the parasites. As soon as I was appointed the Physician-in-Chief of the Government Hospital at Shinchiku, I began to search for the intermediate hosts.

As the first step the development of the eggs and the processes of hatching were studied, but efforts at experimental infection of animals both per os and subcutaneously with the miracidia were unsuccessful. Hence I concluded that at least one intermediate host functions prior to the infection of man. Various species of mollusks occurring in the local streams were examined microscopically, and seventeen different kinds of cercariae were found, but it could not be determined which represented those of Paragonimus westermanni.

The next step was to ascertain which mollusks the miracidia of pulmonary distomas infest. For this purpose various kinds of fresh water mollusks were kept in water in which the miracidia had been made to hatch; and it was soon found that the miracidia prefer Melania libertina and Melania obliquegranosa. Attempts to keep the mollusks alive in aquaria failed. From the fact that the only species of fresh water mollusks that live in the thickly infected regions
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is *Melania libertina* Gould, it was assumed that the cercariae with a characteristic organ in the oral sucker found in the snail must be the young of the pulmonary distomas. But how the miracidia find their way into the mollusks and develop into cercariae has not as yet been ascertained.

Because of the difficulty of verifying this assumption experimentally an effort was made to discover the second intermediate host according to Kobayashi's (5) method employed in human liver distomiasis. This consists in infecting animals with the young distomas occurring in certain fish. After many attempts I found in Kalapai, in September, 1914, many encysted cercariae in the liver and gills of certain crabs, which bore a striking resemblance to mature pulmonary distomas. I finally succeeded in discovering their path of penetration to the lungs of the final host. The facts that the cercariae mentioned above enter the second intermediate hosts, i.e., the crab, and that the cercariae embedded in *Melania libertina* are the cercariae of *Paragonimus westermani*, have now been satisfactorily established.

*Development of the Worm within the Egg.*

Observations on the development of the worm within the egg have already been made by Nakahama, Manson, and Garrison and Leynes, in Japan, China, and the Philippines. The procedure that I employed for the Formosan form is as follows: A quantity of expectorated sputum containing the eggs is placed in a glass dish which is filled with water to the depth of 20 to 30 mm. The vessel is left uncovered in a dark place, and the water changed daily. The sputum and eggs sink to the bottom of the vessel and are readily examined microscopically. Too much sputum is to be avoided as the development of the egg is hindered; test-tubes are unsuitable as the worms do not hatch well.

The egg of *Paragonimus westermani* in fresh sputum is oblong (0.063 to 0.084 by 0.045 to 0.054 mm.) and yellowish brown (Fig. 1). It has an operculum at one end and contains an embryo and several yolk cells (Fig. 2). The yolk cells gradually enlarge and the granules manifest Brownian movement which lasts until the yolk cells are completely taken up by the embryo. At the ten cell stage

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1 These will be described fully below.
or a little later, the cell boundaries become indistinct. When the miracidium is about visible (Fig. 3), the yolk granules are diminished, and the contents of the egg become clearer. The rounded end of the ovoid embryo is directed toward the operculum and the oral part develops at that end (Fig. 4). At this stage the embryo resembles a melon seed and is covered with fine cilia. A few days later the embryo takes on a slow vermicular motion, becoming gradually more active until the miracidium bends upon itself. The cilia cover the surface of the body except the oral part, and are longest over the anterior part, especially about the protruding anterior end. They point posteriorly, except near the oral part where the direction is reversed. Through the vigorous movement of the cilia of the miracidium the operculum is torn off and the embryo is set free in the water (Fig. 5).

The egg containing the full grown miracidium measures 0.0792 to 0.09 by 0.0486 to 0.0567 mm., which is larger than that seen in the sputum. The mature miracidia measure 0.0612 to 0.072 by 0.036 to 0.045 mm.

The rate of development of the miracidia varies with the temperature and is retarded by cool weather. During the summer in Shinchiku, i.e., from May to October, melon seed-like miracidia develop in 14 to 15 days, begin to move in 19 to 22 days, and hatch in 23 to 28 days. In March and April they take some weeks to hatch, and the miracidia remain for a long time within the egg even though they are as lively as in the warm season. From November to February or March no development was noted, though the eggs were watched constantly. According to my observations, the temperature for hatching is 25-31°C., and embryonic development ceases below 25°C. Manson (6) gives 26-34°C., Nakahama (7) 30°C., and Garrison and Leynes (8) 25-34°C. At 37°C. the eggs seem to disintegrate. The incubation period in summer is variable even in the same culture. Some eggs hatch in about 3 weeks, others as late as from 5 to 8 weeks. This difference may be due to other causes than temperature; possibly the length of time elapsing since the eggs were passed by the adult worm in the lungs of the patient before they were ejected with the sputum plays a part.

The miracidium when hatched measures 0.081 to 0.099 by 0.036 to 0.054 mm. It is provided with an alimentary tract and ganglion, two flame cells, and numerous granular embryonic cells. As it swims, the anterior end may not be pointed but invaginated. It can be kept alive for only a short time. In several hours its motion becomes sluggish and it assumes a ball-like appearance. Then it moves with a spiral motion and soon becomes inactive and dies.

Garrison states that direct sunlight is injurious to the miracidia. I also observed that embryonic development is arrested even in diffused light if this is intense. On the contrary, if the culture is kept in the dark, development goes on vigorously. Oxygen seems to be necessary for the development of the embryo. The vessel containing the eggs must be kept uncovered, and care should be taken.
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to change the water at least once a day. The eggs contained in
sputum gradually become brown and die if dried, a space forming
between the egg membrane and the shell. If the miracidia either
within or without the egg membranes are subjected to 1 per cent
hydrochloric acid, movement ceases and they die. It is known that
they cannot resist the gastric juice.

In October, 1913, I introduced a quantity of water that contained
full grown miracidia, either swimming free or still in the egg, into
the stomach of pups; other pups were placed in the water containing
free swimming miracidia. In neither case were the animals found
to be infected by distomas, when killed and examined 45 to 100
days later. The miracidia appear to be unable to enter the animal
body either \textit{per os} or subcutaneously, unless they go through the
second intermediate hosts.

\textit{The First Intermediate Host and the Cercaria of Paragonimus
westermanni.}

The cercariae of \textit{Paragonimus westermanni} were detected in the
following three species of fresh water snails.

1. \textit{Melania libertina} Gould (Fig. 20, a), which lives in pools or
sluggish streams. In the villages of the savage mountain tribes,
this species alone was found. Larger specimens than those seen in
Shinchiku occur commonly in the main islands of Japan.

2. \textit{Melania obliquegranosa} Smith (Fig. 20, b), which thrives in
slowly flowing streams, is common in the flat region of Shinchiku.

3. \textit{Melania tuberculata} Mueller, which occurs rarely in Shinchiku.

All the larger specimens of \textit{Melania libertina} collected in the savage
villages where pulmonary distomiasis occurs abundantly were
found to be infected with the cercariae. The occurrence of the cer-
cariae in \textit{Melania obliquegranosa} collected in the lowlands parallels
with the degree of infection. Cercariae were found in only one speci-
men of \textit{Melania tuberculata}, collected in Runasho village.

When the snails are placed in water containing miracidia, the
latter swarm around them and become attached to the heads, jaws,
and feet, and but rarely to the tentacles and mantles. They cling with
their suckers, insert probosces into the tissues of the host and en-
ter the body of the snail like the cercariae of *Schistosomum japonicum*, as described by Miyairi (9). Unlike the miracidia of *Schistosomum*, those of the pulmonary distoma shed their cilia in this act.

The cercaria measures 0.12 long by 0.09 mm. wide, and its tail is 0.054 mm. long. The oral sucker, 0.036 by 0.032 mm. in diameter, is provided with two pear-shaped bodies, the apices of which point posteriorly. It also has a spine, which appears to have a ring on its point. The posterior sucker is smaller than the oral one, having a diameter of 0.018 mm. The cercaria has three pairs of poison glands. The excretory vesicle of the glands is heart-shaped (Fig. 9).

Besides the cercariae, sporocysts of various sizes are found abundantly in the liver of *Melania*. They are sometimes found in the heart and kidneys (Figs. 6 to 8, and 33).

The cercariae mentioned have been detected in several specimens of *Melania* that thrive in the infected regions of the Prefectures of Niigata, Gifu, Tokushima, and Okayama on the main island of Japan.

The identification of the cercariae with those of *Paragonimus westermani* is based on the following data.

1. Only the cercariae under consideration are found in the most thickly infected regions, among the savage tribes.
2. The miracidia of *Paragonimus westermani*, which usually develop into the cercariae described above, can enter *Melania* only.
3. The shape of the spine of the oral sucker of the encysted cercaria in the crabs, and of the excretory vesicle of the young encysted cercaria bears a striking resemblance to those of the cercariae mentioned above.
4. The cercariae successfully infected crabs free from distomas and developed into the specific encysted cercariae.

The last fact seems to be the strongest evidence. The aquarium used for the experiment was a wooden box 3 feet long and 2 feet high. Three sides were completely covered by a thin cloth in order to prevent the intrusion of cercariae from without. Of course, prior to the experiment it was ascertained that the cloth did not allow cercariae to pass through. The cloth was covered by wire netting with meshes of ½ mm., in order to protect it from being torn by the crabs. The bottom of the box was covered with sand and pebbles. The aquarium was placed in a stream so that the crabs might be kept in as natural a condition as possible. Some snails that had been shown to contain the cercariae were kept with the distoma-free crabs for a time. Non-infected crabs were difficult to obtain. I failed
to secure distoma-free crabs from the streams that run through Formosa, even in those regions where pulmonary distomiasis does not occur. Finally I succeeded in collecting young Potamon (Geothelphusa) obtusipes and Potamon (Geothelphusa) dehaanii, and fifty specimens of the former and twenty of the latter were examined and found to be free from the encysted cercariae. On September 4, 1915, the crabs and Melania were put together in the aquarium in the stream. Examinations were made daily. Most of the crabs climbed up the walls and were outside the water. Both the crabs and the snails began to die one after another. On October 10, 1915, I examined twenty specimens each of Potamon obtusipes and Potamon dehaanii. None of the former had encysted cercariae, but one of the latter showed a few, some of which had not been in the host for many hours. 3 weeks later thirty-five specimens of Potamon dehaanii were examined, and three were found to be infected by young encysted cercariae. The experiments are being continued.

Five young specimens of Potamon obtusipes and of Potamon dehaanii were placed in a vessel filled with water containing a large number of cercariae, obtained by crushing snails. In 3 days one of the former species was found to harbor a few encysted cercariae. It is evident that the infection occurred in the vessel; for the embedded, encysted cercariae were so young that they could not have been many hours in the host. The reason why so few crabs become infected experimentally may be due to differences in environmental conditions.

Crabs as the Second Intermediate Host.

Seven species of fresh water crabs collected in the infected and non-infected regions were examined for encysted cercariae. The following three species contained them.

1. Potamon (Geothelphusa) obtusipes Stimpson (Fig. 21), which is the first species in which the encysted cercariae of Paragonimus westermani were found, and which has only been found in the mountainous regions of Shinchiku. It seems probable that this species is peculiar to the regions mentioned above, though Stimpson points out that specimens collected in the island of Amamioshima in the Prefecture of Kagoshima are identical with them.

I found this species abundant in the streams running through the mountainous regions in the Prefecture of Shinchiku, and also present in the mountainous regions of Usekiko village in the Prefecture of Taichu and Chikutoki village in the Prefecture of Kagi. The occurrence in this species of encysted cercariae corresponds with the degree of infection. Among the savages, where 30 to 50 per cent of the
population suffer from the infection, 80 to 100 per cent of this species harbored encysted cercariae. Moreover, in Kalapai village, in which 55 per cent of the inhabitants suffer from pulmonary distomiasis, all the crabs harbored encysted cercariae; while only 11 per cent of the crabs from the creeks of Naiwan, situated about 4 miles away, showed encysted cercariae. The inhabitants of the latter village are believed to have the disease but rarely. In Sansaka, where distomiasis seldom occurs, the crabs showed no encysted cercariae.

2. *Potamon* (*Geothelphusa*) *dehaanii* White (Fig. 22), which is found in the same locality, but less abundantly than the preceding species.

3. *Eriocheir japonicus* De Haan (Fig. 25) which, unlike the two species mentioned above, never occurs in the streams of the mountainous regions, but is found in the rivers flowing across the plain.

300 large specimens and over 30 small specimens were examined microscopically in February, 1915, for encysted cercariae. Of these only two showed, in the gills, one encysted cercaria each. At first it was suspected that this was accidental, but later I learned that cercariae may be found, though rarely, in the gills and muscles of this crab in the village of Torunsho.

Thus it seems to have been conclusively demonstrated that these three species of fresh water crabs act as the intermediate host of *Paragonimus westermanii*; the first species showed the largest percentage of infection, the second a much smaller percentage, while the third was but rarely infected. The first species is found exclusively in Formosa, while the second and third are found also in other parts of Japan. I came, therefore, to the conclusion that these last two species play the part of the second intermediate host in the main islands of Japan.

Recently, Kobayashi (10), Ando (11), and Yoshida (12) demonstrated that the second species is the intermediate host in the infected regions in the Prefectures of Niigata and Gifu, and the third species in the Prefecture of Tokushima, and both the second and third species in the Prefecture of Okayama. Yoshida (12) claims that another species of crab, *Sesarma dehaanii* Milne-Edwards (Fig. 24), is the second intermediate host in the village of Hiyeshima in Nishinaru County in the Prefecture of Osaka. This species is also found in the region near the sea in the Prefecture of Shinchiku in Formosa, but no encysted cercariae are
found in it. Moriyasu, Arima, and Tanakamaru (13) lately detected a species of crab that harbors encysted cercariae, of which they kindly sent me specimens. Upon examination, they were found to belong to the third species described above. Professor Miyairi of the Kyushu Imperial University also found that Astacus japonicus DeHaan is the intermediate host of Paragonimus westermanni in Korea. In one of the infected regions in Formosa, i.e., in the village of Shinko, Prefecture of Taiboku, the third species as well as another variety, Potamon (Parathelphusa) sinensis Milne-Edwards (Fig. 23), was found by Yokokawa (14) to have encysted cercariae. The following table shows the species and the localities in which they act as second intermediate hosts.

<table>
<thead>
<tr>
<th>Species</th>
<th>Prefecture</th>
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<tbody>
<tr>
<td>1. Potamon (Geothelphusa) obtusipes Stimpson</td>
<td>Shinchiku</td>
</tr>
<tr>
<td>2. Potamon (Geothelphusa) dehaanii White</td>
<td>Niigata, Gifu, Okayama</td>
</tr>
<tr>
<td>3. Eriocheir japonicus De Haan</td>
<td>Shinchiku, Tokushima, Okayama, Korea</td>
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<tr>
<td>4. Sesarma dehaanii Milne-Edwards</td>
<td>Osaka</td>
</tr>
<tr>
<td>5. Astacus japonicus De Haan</td>
<td>Taihoku</td>
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<tr>
<td>6. Potamon (Parathelphusa) sinensis Milne-Edwards</td>
<td>Taihoku</td>
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Encysted Cercariae of Paragonimus westermanni in Crabs.

The size and shape of encysted cercariae vary with their age. The younger ones are found embedded chiefly in the liver, while the older ones occur either in the liver, the gills, or even in the muscles. In the liver, they lie exclusively in the interspace of tissue.

1. Youngest Forms.—The youngest forms (Figs. 10 and 11) are not commonly detected in the crab, as the cercariae usually enter at night. The youngest individuals present in the crabs were found at 5 o'clock in the morning just pushing their way into the parenchyma of the liver. They measured 0.13 by 0.05 mm. and had no tail. The posterior part is narrower than the anterior; they possess an oral sucker (0.04 mm. in diameter), and a spine in the oral sucker, which corresponds with that observed in the encysted cercariae, except that it has no ring and a small posterior sucker (0.02 mm. in diameter) situated in the middle of the body. There is no excretory vesicle. In the anterior part of the body there is a tube-like organ which looks like the duct of poison glands. The worm appears as a white speck on the yellow parenchyma of the liver.

Immediately before transformation into encysted cercariae the individuals are rarely seen, but not so rarely as the preceding stage. They now are folded on themselves and contract and extend their heads alternately but remain fixed...
to the same spot. A little later a thin cyst, 0.11 mm. in diameter, encloses the worm, and within it the larva moves (Fig. 12). In still further advanced stages the cyst measures 0.13 mm. in diameter, the oral sucker is smaller, and a lumen (probably the pharynx) is seen immediately posterior to the latter. The posterior sucker has now enlarged slightly, while at the posterior extremity and along the median plane a rudimentary excretory vesicle, which sends off branches parallel to the axis of the body, has appeared (Fig. 13). Still later the cyst measures 0.14 mm. in diameter and there is a wider excretory vesicle, filled with coarse granules (Fig. 14). Finally, the larvae lie straight within the cyst, the excretory vesicles gradually become heart-shaped, and fine dark granules appear and soon assume the form to be described.

2. Young Cercariae (Figs. 15 to 18).—The young cercariae possess a cyst measuring 0.18 to 0.2 mm. in diameter in which they lie extended. They have a large black excretory vesicle, and relatively large oral and posterior suckers, which tend to assume an ellipsoidal shape due to pressure. The oral sucker is 0.035 to 0.042 mm. long and 0.05 to 0.056 mm. wide, while the posterior sucker is 0.035 to 0.043 mm. long and 0.052 to 0.057 mm. wide. The spine of the oral sucker is present though it can be detected only with difficulty. No alimentary canal is differentiated. The cyst consists of chitin which is 0.005 to 0.006 mm. in thickness.

The young encysted cercariae can be seen by the naked eye, in a piece of liver crushed between two slides, as small white dots lying between the lobules.

3. Full Grown Cercariae (Figs. 19 and 34).—These are contained within a cyst from 0.26 to 1.0 mm. in length and 0.4 mm. in width. The oral sucker measures 0.07 to 0.09 mm. in diameter. The black-appearing intestinal canals are thick and wind on both sides of a large excretory vesicle. The posterior sucker (0.09 to 0.11 mm. in diameter) is a little larger than the oral one, and tends to be hidden by the excretory vesicle. The whole surface is covered with short cilia. The thick cyst, measuring 0.01 to 0.014 mm., is one of the characteristics of the species. The cercariae move sluggishly within them. The liver usually contains three to four and never more than ten. The muscles contain few cercariae; the gills contain the most. In the gills of one crab 97 full grown cysts were found. The cercariae in this stage are detached from the gills and 20 per cent are found floating in the water. Under natural conditions they seem to leave the gills and drift along the streams, which thereby become a source of infection for human beings.

The above observations were made chiefly on Potamon obtusipes. In P. dehaanii and Eriocheir japonicus the development takes place in a similar way.

Experimental Infection with the Encysted Cercariae.

In order to determine to what species the encysted cercariae in the crab belong, tests were conducted on dogs. Pups born in the
regions in which pulmonary distomiasis does not occur were chosen, since dogs are liable to infection under natural conditions. Two pups were fed twice, on September 23, and October 10, 1914, with large quantities of the gills and livers of crabs containing encysted cercariae. One of them died on December 9, 60 days after the last feeding.

Numerous cysts were found in the lungs. Each cyst showed two or three full grown distomas that contained no eggs in the uterus. They were 4 to 5 mm. long by 2 to 3 mm. wide. The other animal died on December 25, 75 days after the last feeding. Numerous cysts containing egg-bearing distomas were found in the lungs. The worms were 6 to 7 mm. long and 3 to 4 mm. wide, just one-half the size of the worms of spontaneous infection in the cat and dog and in man, but morphologically they were identical with *Paragonimus westermanni*.

The experiment was repeated on two pups from a non-infected region (December 26, 1914, to February 7, 1915) with identical results. On another occasion animals were given water containing the encysted cercariae which had been detached from the gills of the crab, and adult distomas developed also in these animals.

*The Course of Penetration of the Cercariae in the Final Host.*

Since the distomas appear to reach their destination in the final host by passing through the walls of the alimentary tract, the next step was to make clear their course. Microscopical examination of the viscera of the infected animals indicated that the distomas passed through the walls of the alimentary tract and the diaphragm, and thus reached the lungs. Yamagiwa (15) believes that the distomas reach the lungs by way of the liver, and then by the diaphragm, the pleura, etc., since adherent nodules involving these organs have been demonstrated. My observations were made in the early stages, so that congestion and hemorrhage of the mucous membrane of the intestine could be detected as well as petechiae in the diaphragm and lungs, especially the lower lobes. By studying the petechiae, points were found through which the worm seemed to have passed. At this early period I concurred with Yamagiwa's views. Just at
this juncture Yokokawa (14) discovered many distomas floating in the serous exudates of the abdominal and thoracic cavities of dogs to which encysted cercariae had been fed.

At the suggestion of Dr. Miyajima of the Kitasato Institute, I examined a dog and a cat sent from Shinchiku where they had been fed encysted cercariae, for more than 10 days, and succeeded in determining the path of penetration.

Experiment 1.—A pup was fed from April 15 to 27, 1915, large numbers of crabs gathered in the savage villages. The animal died on April 27. The body cavity was opened and the animal immersed in 10 per cent formalin.

Macroscopical examination showed petechiae in the mucous membrane of the intestine near the jejunum. The other abdominal viscera and the diaphragm presented no changes. The lungs showed general pneumonic areas. Since this condition was not met with in other cases it must be regarded as a complication.

Nearly the whole omentum was sectioned, and several worms were found: one (0.22 by 0.14 mm., smaller than usual owing to the fixation) in the parenchyma of the omentum near the greater curvature of the stomach, another (0.36 by 0.24 mm.) in the fat tissue, and others in the diaphragmatic ligament where the worms (0.3 by 0.18 mm.) were surrounded by hemorrhage. No worms were found in the liver or the mediastinum, and none were detected in the lungs. Similarly, the contents of the lymphatic system, the thoracic cavity, and the heart were negative.

Experiment 2.—A cat was fed for 15 days with a large number of encysted cercariae (April 18 to May 2, 1915), when it was chloroformed, the body cavity opened, and the animal placed in formalin.

On macroscopical examination petechiae of various sizes, some as small as 1 mm. in diameter, were found in the mucous membrane of the jejunum (Fig. 26). A note by the collector of the material stated that four or five grayish white vesicles were present on the diaphragm, which undoubtfully were worms. Small petechiae were present in the capsule of the spleen, and in the muscle of the diaphragm. The surface of the lungs, especially the lower lobes, showed many petechiae.

Sections were made through the basal part of the omentum, the liver, the ligament and tendinous part of the diaphragm, and the mediastinal tissues, but no worms were found. Large portions of the lungs were sectioned and worms were found entering the pleura on their way to the parenchyma of the lungs. In sections made through the jejunum a worm (0.28 by 0.18 mm.) was found that had just entered the external layer of muscle. This path was indicated by the torn muscle fibers, the infiltrated round cells, and especially the eosinophil cells (Fig. 35). No worms were found in the cecum; hence they must have dropped when the material was fixed. Worms could not be detected in the act of piercing
the lungs. However, in an experimental animal 7 weeks after the feeding, a worm (2.2 by 1 mm.) that had already reached the parenchyma of the lungs was found. Thus, it may be said that the path by which the worm reaches the lung parenchyma has been ascertained.

In brief, the results of my observations support Yamagiwa’s view; for they establish the point that cercariae of *Paragonimus westermanni* taken *per os*, with the food, pierce the intestinal wall, pass into the abdominal cavity, then through the diaphragm into the thoracic cavity, and finally reach the lungs, where they produce cysts and grow into adults.

Since my discovery, Yokokawa (16) has also reported in several papers, published in Japanese, minute observations on the same subject, and they have been further supported by Kobayashi (10) and Ando (11).

Additional experiments were carried out in Formosa, of which illustrative protocols are here given.

*Experiment 3.*—From April 18 to May 16, 1915 (29 days), a kitten 2 was fed with many encysted cercariae and then killed for examination. The mucous membrane of the intestines was found to be congested, and several petechiae were seen in the jejunum. Several worms were attached to the omentum. The liver was hyperemic, and the upper portion in apposition with the diaphragm was perforated by small pores that reached the parenchyma, in which young distomas were seen wriggling in and out. Many younger ones were also attached in the same region. Several worms were attached to the liver and the ligament of the diaphragm, while some were seen crawling on the lower surface of the diaphragm itself (Fig. 28). The capsule of the spleen presented several cyst-like protuberances and some petechiae. The kidneys were normal. By washing the abdominal cavity with saline solution, sixteen young distomas were obtained. From the liver and the diaphragm, eleven worms were obtained.

In the thoracic cavity about 30 cc. of bloody turbid fluid were present, which contained one worm. The parietal pleura showed many cysts and petechiae. On the thoracic aspect of the diaphragm many punctures and hemorrhagic spots were seen and some worms were present in the muscle layer (Fig. 36).

*Experiment 4.*—From April 28 to May 16, 1915 (19 days), a kitten 2 was fed on crabs collected among the savages. The surface of the liver and diaphragm showed numerous perforations in which were young wriggling worms. The muscular layer of the diaphragm was the

2 These two animals were examined by my assistants in the Shinchiku Hospital during my stay in Tokyo.
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seat of several hemorrhagic spots, as was also the visceral pleura. Thirty-six worms were found in the celom, and thirty-five on the surface of the liver.

Experiment 5.—100 mature encysted cercarids were fed per os to a kitten at 10 a.m. and 4 p.m. on June 26, 1915. The animal was killed 6 hours later.

There were about 20 cc. of light yellowish fluid in the abdominal cavity; no worms were found. In the upper part of the ileum a young distoma that had just come out of the cyst, and another still in the cyst, were found; in the jejunum were found numerous specimens of Ascaris mystax. The other organs were normal. The fluke found in the ileum measured 0.35 by 0.21 mm. The empty cyst measured 0.28 mm.

Experiment 6.—A kitten was fed with 100 full grown encysted larvae at 3 p.m. on June 27, 1915, and killed for examination at 2 p.m., July 17; that is, 3 weeks after the feeding.

The animal was somewhat emaciated. The abdominal cavity contained a small quantity of cloudy fluid; no worms were found. The serous membrane of the intestine was congested. One worm was attached to the surface of the liver. Three worms were seen moving on the abdominal surface of the diaphragm. A worm was found at the greater curvature of the stomach, but no worms were free within the abdominal cavity.

The thoracic cavity contained a large quantity of cloudy reddish fluid from which twenty worms were obtained. Two worms were attached to the heart. Many worms were found on the pleura where the sternum comes in contact with the pleural diaphragm. The lungs presented a light reddish color with a few scattered hemorrhagic spots. In the central portion of the lower lobe of the left lung one grayish cyst as large as the tip of the small finger was found. One or two worms were seen intruding into the pulmonary pleura, with here and there cyst-like protuberances.

The worms in the thoracic cavity and in the abdominal cavity are identical. The largest specimen measured 2.2 by 1.4 mm., and the smallest 1.1 by 0.8 mm.

Experiment 7.—A kitten was fed 200 full grown encysted larvae at noon on July 1, 1915, and died at 6 p.m. on July 19, 19 days after the feeding. Most of the encysted larvae fed were taken from the gills of somewhat decomposed crabs.

Emaciation; the abdominal cavity contained a small quantity of fluid. The intestinal serosa was slightly congested. One worm was attached to the upper parietal pleura; two worms were found on the liver, one attached to the serosa of the stomach, and another to the serosa of the duodenum. A very small worm was free within the abdominal cavity. The surface of the liver showed a number of vermicular scars. Two worms were penetrating the capsule of Glisson. One worm was attached to the esophagus. In the right lung were seen three somewhat large hemorrhagic spots. Within the pleural cavity opposite the sixth right intercostal space within a hyperemic area a worm lay wedged (Fig. 30)

No difference in size was noted between the worms in the thoracic and in the abdominal cavities. The largest specimen measured 1.5 by 0.7 mm., the smallest 1.0 by 0.6 mm.
Experiment 8.—A pup was fed with 227 full grown encysted larvae at 8 p.m., July 8, 1915, and died at about 2 a.m., July 14, or 126 hours after the feeding. A large quantity of light yellowish fluid containing two or three worms was found in the abdominal cavity. The intestines showed here and there ulcerations in the mucous membrane and innumerable *Ankylostoma caninum*. The stomach contained numerous ascarides. The liver showed two or three hemorrhagic spots, and similar areas occurred in the muscular layer of the diaphragm.

The thoracic cavity contained a large quantity of light yellowish fluid and a few worms. The lungs appeared pale, and a few hemorrhagic spots were seen. The worms in the abdominal and thoracic cavities were generally small, measuring 0.4 to 0.5 mm. by 0.2 to 0.3 mm.

Experiment 9.—A pup was fed fifty full grown encysted larvae at 7 a.m., July 9, 1915, and died August 2; that is, 25 days after the feeding. The abdominal cavity was free from fluid. One distoma was attached to the upper left quadrant of the parietal peritoneum. The liver was hyperemic and showed a few serpentine scars on the surface. One worm was attached to the omentum. A few hemorrhagic spots were seen in the muscular layer of the diaphragm.

In the right thoracic cavity was a small quantity of bloody turbid fluid; there was none in the left. On the abdominal aspect of the diaphragm one active worm was seen, and another in the diaphragmatic ligament. The lungs showed numerous hemorrhagic spots but no cysts (Fig. 31).

The largest worm measured 3.0 by 1.2 mm., and the smallest 1.2 by 0.6 mm.

Experiment 10.—On September 9 and 10, 1915, a pup was fed 30 and 40 full grown encysted larvae respectively, collected in a savage village. The animal was killed 45 days after the last feeding.

No fluid was present in the abdominal cavity. One worm was found on the abdominal surface of the diaphragm and another on the diaphragmatic surface of the liver. Both were small.

No fluid was present in the thoracic cavity. One worm was attached to the mediastinal tissues, and one to the pericardium. The lungs were reddish purple in color, and showed numerous dark brownish red hemorrhagic specks and gray cyst-like scars. The right lung contained about ten cysts, the left only one.

The largest worm measured 4.5 by 2.2 mm.; and the smallest was about one-half that size.

Experiment 11.—In order to determine whether the hairy crabs are the intermediate host of the worm, a pup was fed 200 crabs between July 27 and August 23, 1915, after the carapace and the legs had been removed, and the viscera and the muscles minced. The animal died at midnight on August 24. The crabs were bought in the market of Shinchiku and given to the animal without examination for the presence of the larvae.

On the surface of the liver were one or two small hemorrhagic spots. In the right thoracic cavity was a small quantity of bloody fluid. One worm was attached to the lower lobe of the right lung, and one was seen crawling over the thoracic surface of the diaphragm. The lungs were pale with occasional large
dark bloody flecks, some of which had a wound in the central part where the parenchyma had been injured. In the inferior lobe of the right lung was seen a small dark red nodule, which had a small cavity in the center from 5 to 7 mm. in diameter and 12 or 13 mm. deep, at the bottom of which a worm was found.

In the ligament of the diaphragm were seen three small perforations the size of a pin-head. In the muscular layer of the diaphragm one or two hemorrhagic spots were present.

The worms in the thoracic cavity measured 3.0 by 1.5 mm., while those in the abdominal cavity measured 2.4 by 1.2 mm.

This experiment indicates that the hairy crabs may also act as the second intermediate host of *Paragonimus westermanni*.

Eighteen animals were employed in the experiments, eleven of which are reported above.

The animals were given *per os* a comparatively small number of encysted larvae, usually about 100. There developed in consequence mild infections with slight pathological changes.

Table I gives the results obtained.

**TABLE I.**

*Results of Feeding Encysted Larvae of Paragonimus westermanni to Kittens and Pups.*

<table>
<thead>
<tr>
<th>Experiment No.</th>
<th>Species</th>
<th>Time between feeding and examination</th>
<th>No. of worms</th>
<th>Size of worms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kitten</td>
<td>6 hrs.</td>
<td>2</td>
<td>0.35 X 0.21</td>
</tr>
<tr>
<td>2</td>
<td>&quot;</td>
<td>16 &quot;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>&quot;</td>
<td>1 day.</td>
<td>2</td>
<td>0.3 X 0.15</td>
</tr>
<tr>
<td>4</td>
<td>&quot;</td>
<td>2 days.</td>
<td>1</td>
<td>0.73 X 0.21</td>
</tr>
<tr>
<td>5</td>
<td>&quot;</td>
<td>24 days.</td>
<td>1</td>
<td>0.5 X 0.22</td>
</tr>
<tr>
<td>6</td>
<td>Pup.</td>
<td>3 days, 15 hrs.</td>
<td>2</td>
<td>0.53 X 0.33</td>
</tr>
<tr>
<td>7</td>
<td>&quot;</td>
<td>5 &quot; 6 &quot;</td>
<td>5-6</td>
<td>0.4-0.5 X 0.2-0.3</td>
</tr>
<tr>
<td>8</td>
<td>Kitten</td>
<td>14 &quot;</td>
<td>8</td>
<td>0.73-1.47 X 0.44-1.1</td>
</tr>
<tr>
<td>9</td>
<td>&quot;</td>
<td>18 &quot;</td>
<td>11</td>
<td>1.5-1.0 X 0.7-0.6</td>
</tr>
<tr>
<td>10</td>
<td>Pup.</td>
<td>21 &quot;</td>
<td>Over 25.</td>
<td>2.2-1.1 X 1.4-0.8</td>
</tr>
<tr>
<td>11</td>
<td>&quot;</td>
<td>25 &quot;</td>
<td>4</td>
<td>3.0-1.2 X 1.2-0.6</td>
</tr>
<tr>
<td>12</td>
<td>&quot; *</td>
<td>45 &quot;</td>
<td>4</td>
<td>4.5 X 2.2</td>
</tr>
</tbody>
</table>

*(Besides numerous cysts.)*

*Experiments in which the animals were kept longer than 45 days after the feeding are described elsewhere.*

*With the exception of Experiments 1 to 4 and 11, cercariae were given to the subject only once.*
KOAN NAKAGAWA

The following conclusions have been reached. Encysted larvæ taken *per os* by the final host reach the jejunum, where they emerge from the cysts and make their way through the intestinal epithelium into the submucosa (Figs. 26 and 35). From that structure they pierce the muscular layer and pass into the abdominal cavity. This process required, in the earliest case, 24 hours. Some larvæ remain in the intestines for 10 hours or more. Once in the abdominal cavity the worms proceed upward along the mesentery and the omentum and reach the liver (Figs. 27, 29, and 37), where they become attached to the diaphragm which is pierced at the ligament or in the muscular region (Figs. 28 and 36). The first worms pass into the thoracic cavity 77 hours after reaching the alimentary canal, but most of them remain on or in the liver for some time before they reach the thoracic cavity.

Some fail to reach the lungs, and, as Yokokawa believes, remain in the mesentery, the omentum, and the seminal ducts, forming cysts. In the thoracic cavity they often remain in the subvisceral pleural region or in the serous fluid. While in the pleural cavity they seem to grow before they enter the lung parenchyma where sooner or later they form cysts. It is doubtful whether they remain in the pleural cavity for a long time without forming cysts.

The changes in the lungs may be summarized as follows (Figs. 31, 32, and 38). 3 days after the feeding, a few pin-head hemorrhagic spots appear in the lungs. They are the beginning of wounds caused by the worms. In about 14 days, some of these spots become dark red, and in 21 to 25 days pale cysts have developed. Usually the cysts correspond in position to the petechie. The following phenomena have also been observed. In some instances, 45 days after feeding the encysted cercarie, on the surface of the lungs numerous small dark-red cysts are formed about which are infiltrations of polymuclear leukocytes or round cells in addition to the red corpuscles. In 50 days the surface of the lungs comes to have numerous dark reddish hard cysts as large as the tip of the little finger. The cut surface of the cyst appears dark red, from a previous hemorrhage; in the center is a vacuole the size of a pea. The distomas when present lie in the vacuole; but empty ones are also observed, for the worms may escape into the neighboring tissues. After about 90
days, the cysts have become bluish gray. On section a vacuole as large as a bean is found, in which porridge-like matter or one or two mature distomas are seen. In the latter case one of the two may be found dead. The walls of the cyst are composed of a thin layer of connective tissue.

The cyst wall may in some regions be wanting, the lumen being connected directly with the air spaces, a bronchus, or radicle of the pulmonary vein. Thus it is seen how the regional bleeding or pneumonic infiltration of the alveoli originates. Eggs were observed in worms 90 days after the feeding. When they are shed, they lie sometimes in the cysts, but oftener in the parenchyma of the lungs, mingling with the erythrocytes and leukocytes, epithelial cells of the lungs, or cellular detritus, etc. The bronchi and bronchioles near the lesions are dilated and contain erythrocytes or leukocytes together with eggs. The microscopical changes described indicate that the worms do not always remain within the cysts, but may emigrate into other parts of the lungs.

*Development of Cercaria in the Final Host.*

The size of the distoma depends upon (a) the initial size of the cercariae and (b) the nutriment. The following figures give the measurement of specimens fixed with alcohol.

**TABLE II.**

*Size of Paragonimus westermanni at Various Ages.*

<table>
<thead>
<tr>
<th>Age, days</th>
<th>Length</th>
<th>Breadth</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mm.</td>
<td>mm.</td>
</tr>
<tr>
<td>Just hatched</td>
<td>0.3 -0.48</td>
<td>0.18-0.23</td>
</tr>
<tr>
<td>3</td>
<td>0.44-0.48</td>
<td>0.23-0.26</td>
</tr>
<tr>
<td>6</td>
<td>0.44-0.53</td>
<td>0.26-0.32</td>
</tr>
<tr>
<td>14</td>
<td>0.65-0.95</td>
<td>0.37-0.61</td>
</tr>
<tr>
<td>18</td>
<td>0.8 -1.6</td>
<td>0.4 -0.85</td>
</tr>
<tr>
<td>21</td>
<td>1.3 -2.0</td>
<td>0.8 -1.1</td>
</tr>
<tr>
<td>25</td>
<td>0.9 -2.2</td>
<td>0.7 -1.3</td>
</tr>
<tr>
<td>45</td>
<td>2.5 -3.5</td>
<td>1.5 -2.0</td>
</tr>
<tr>
<td>60</td>
<td>4.0 -5.0</td>
<td>2.0 -3.0</td>
</tr>
<tr>
<td>90</td>
<td>6.0 -7.0</td>
<td>3.0 -4.0</td>
</tr>
</tbody>
</table>
Young worms (Figs. 39 to 42) have relatively large suckers, as shown by the measurement of fresh specimens. The larvae which have just left the cysts present an oral sucker whose diameter is 0.07 to 0.09 mm. and a ventral sucker 0.09 to 0.11 mm. in diameter. In a 14 day old specimen (i.e., after the feeding) the oral sucker is 0.14 to 0.23 mm. and the ventral sucker 0.16 to 0.26 mm.; in 21 day old specimens the oral sucker is 0.22 to 0.33 mm. and the ventral sucker 0.23 to 0.36 mm.; in those 45 days old the oral sucker is 0.3 to 0.5 mm. and the ventral 0.33 to 0.53 mm. in diameter.

The encysted cercariae have a large excretory vesicle, occupying nearly the whole central body space, which is filled with a black granular substance. In the final host the contents escape and the vesicle becomes a small dark-appearing space.

The development of the genital organs takes place slowly. In a young worm just out of the cyst, the gonads are hardly visible. In a 2 week specimen gonial regions appear which are deeply stained by borax carmine. In 18 to 21 day specimens the differentiation of the ovaries and the uterus has taken place. The ootypes appear as small groups of cells, one on each side of and posterior to the ventral sucker. The uterus is a simple winding tube. The testes make their appearance at a region corresponding to the ovaries. In a 25 day specimen (Fig. 42) both the ovaries and the testes have sent out several branches. In 50 day specimens (Fig. 43) the gonads are mature, but the yolk glands are not yet fully developed. The 90 day specimens (Fig. 44) lay eggs and have mature yolk glands. To sum up, within 3 weeks the rudimentary genital organs make their appearance and within 3 months they begin to function.

**Resistance of the Encysted Cercaria to Environmental Influences.**

It is of importance for the prevention of pulmonary distomiasis to determine the power of resistance of encysted cercariae to external influences.

Young encysted cercariae are so delicate that they die in a few hours after becoming detached from a crab. They never develop in the final host, a fact experimentally proved by feeding them to a dog.

If full grown encysted cercariae are artificially removed from the gills of the crabs and put into clear water, they soon swell and curl within the cysts similarly to other distomas. If the cercariae are small, they remain inactive for a day or two or even longer within the cysts. Encysted cercariae kept in clear water for almost 3 days either remain curled up or develop a remarkably enlarged excretory vesicle and compressed intestine. None wriggled, but one or two dead worms were seen to have shed the cysts. On another occasion
the encysted cercariae still attached to the gills were put into the water and allowed to stand for some time at room temperature (about 30°C.). After 3 days the results were as shown in Table III.

**TABLE III.**

*Behavior of Encysted Cercaria in Water.*

<table>
<thead>
<tr>
<th>No. of gills</th>
<th>Total No. of encysted cercariae</th>
<th>Empty cysts</th>
<th>Dead cysts</th>
<th>Living cysts</th>
<th>Free cercariae</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16</td>
<td>7</td>
<td>3</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>7</td>
<td>5</td>
<td>6</td>
<td>17</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>42</td>
<td>19</td>
<td>6</td>
<td>17</td>
<td>4</td>
</tr>
</tbody>
</table>

From this table it is seen that about half the encysted cercariae hatched, while the other half remained within the cysts although still alive. A few were found dead inside the cysts. The remainder of the cysts, reexamined 5 days later, were found either evacuated or dead.

As Kobayashi (5) has shown with *Clonorchis sinensis*, the encysted cercariae of *Paragonimus westermani* leave the cysts on being kept several hours in fresh water, and the empty cysts are often seen in the alimentary canal of the final hosts, and it may therefore be inferred that the cercariae escape before the cysts are digested in the intestine. In the winter, however, when the temperature in Shinchiku is about 15°C., the cercariae do not escape from the cysts even if kept in fresh water for 2 weeks or more.

The question arises whether the cercariae would infect herbivorous animals since they are liberated without any external agency. Ando (17) reported the successful infection of white mice, guinea pigs, and rabbits, to which encysted cercariae had been fed. I also made experiments upon mice, but have reached the conclusion that the infection seems more difficult to achieve in these small animals than in dogs and cats.
The newly hatched cercariae do not resist even slight temperature changes. In the summer in Shinchiku when the room temperature is about 30°C. they all die in 20 to 30 hours. As long as the encysted cercariae remain in cold streams ready to enter the final host, they do not become liberated. It is of interest from the standpoint of the prevention of distomiasis that the free, living cercariae may be swallowed by man with water or food without harm.

On the other hand, the full grown cercariae are enclosed within cysts much thicker than those of any other known species. The cysts are impermeable to both paraffin and celloidin. The resistance was tested with results which may be stated as follows:

When the crabs containing them are roasted over the fire until the muscles turn white the cercariae are killed. Heating the crabs in water at 55°C. for 5 minutes also destroys them.

Heating the encysted cercariae, removed from the crab, in water at 45°C. for 37 minutes does not kill them, but after heating to 55°C. for 10 minutes or to 70°C. for 5 minutes, they are killed.

The encysted cercariae survive in 1 per cent solution of sodium chloride for 3 hours, or in 10 per cent solution for 2 hours. They first shrink but are soon restored to normal when transferred to fresh water.

The encysted cercariae contained on the crabs' gills were put in soya sauce. At the end of 30 minutes they were alive, but after 9 hours they were killed. 50 specimens of the larger encysted cercariae which had been immersed in soya sauce for 2 hours were fed to a kitten which when killed 3 weeks later was found not to be infected.

Immersion in vinegar for 30 minutes does not kill the cercariae, but immersion for an hour does.

The above experiments may be summarized as follows: The cercariae are liberated under natural conditions, if the temperature is high enough. When hatched they have little power of resistance to injurious influences. Within the cysts, on the contrary, they are hardy and withstand for quite a time immersion in solutions of table salt, soya sauce, and vinegar. Hence, crabs are dangerous unless they have been in soya sauce or vinegar for 2 hours or more after their carapaces are removed. A solution of table salt at the con-

4 This was confirmed by the experiments of Matsui, Y., Biological studies on the cercariae of the pulmonary distoma. Hokuyetsu Igakkwai Zasshi, 1915, xxx, No. 3.
centration used for culinary purposes is not strong enough to kill cercariae. Though the cercariae are not especially resistant to heat, half boiled or half roasted crabs are unsafe as food.

Principal Causes of the Prevalence of Pulmonary Distomiasis and Its Prevention.

It still remains to be determined how human pulmonary distomiasis is caused. At first I entertained the notion, in conformity with that of Ando (11) and Moriyasu, Arima, and Tanakamaru (13), that the encysted cercariae, separated from the gills, which survive for a time on the surface of the water and which may be found free in water in which infected crabs have been, are the sources of infection. But later I concluded that the eating of crabs containing the cercariae is the chief cause of the disease. Of twenty-two patients suffering from the disease, seventeen, or 77 per cent, gave a history of eating hairy crabs and three, or 13.6 per cent, red crabs.

An objection to this view may be found in the fact that only about 0.5 per cent of the crabs are infected. But a similar condition is found in liver distomiasis, for Kobayashi (5) has affirmed that the least infected fish, Carassius auratus, is responsible for most of the hepatic distomiasis. This view is supported by the statement that raw crabs are eaten in some parts of Japan and particularly in the highly infected regions of Korea.

Hence it may be concluded that the eating of raw or imperfectly prepared crabs and the drinking of river water which they inhabit are the two principal causes of pulmonary distomiasis.

Conclusions.

1. The morbidity of pulmonary distomiasis among the school children in the plains of the Prefecture of Shinchiku is 4.3 per cent, while in the mountainous regions among the savages it reaches in some districts 50 per cent.

2. Seventeen species of cercariae were discovered in fresh water mollusks in the Prefecture of Shinchiku, Formosa. But it was impossible to ascertain from morphological characteristics alone which of them developed into the pulmonary fluke. Consequently,
the eggs of the pulmonary fluke after hatching into miracidia were
allowed to come into contact with several species of fresh water
mollusks, of which they infected two. But as it was difficult to keep
the two species alive in the aquarium long enough to get cercariae,
the second intermediate hosts of the pulmonary distomas were looked
for in the severely infected villages of the savage tribes.

3. The miracidia of the pulmonary distomas leave the egg about
4 weeks after they are first set free in the water, and if they do not
reach mollusks they soon die.

4. Three species of fresh water mollusks were found to act as the
first intermediate host of the pulmonary distomas; *Melania
libertina* Gould, *Melania tuberculata* Mueller, and *Melania oblique-
granosa* Smith.

5. The cercariae of the pulmonary distoma may be identified by
their small size and a spine in the oral sucker. They develop in
the liver of the three species of *Melania* mentioned above.

6. The second intermediate hosts of the pulmonary distoma, detected
in the Prefecture of Shinchiku, are the following three species of fresh
water crabs: *Potamon (Geothelphusa) obtusipes* Stimpson (native name,
red crab), *Potamon (Geothelphusa) dehaanii* White (native name, dung
crab), and *Eriocheir japonicus* De Haan (native name, hairy crab). In
addition it was discovered that the following two species might act
as intermediate hosts: *Sesarma dehaanii* Milne-Edwards and *Potamon
(Parathelphusa) sinensis* Milne-Edwards. In Formosa four of the
five species are the carriers of the cercariae.

7. The encysted cercariae are found in the gills, liver, and muscle,
and have an elongated dark excretory vesicle in the middle of their
bodies. They resemble the adult flukes.

8. Full grown encysted cercariae fed to dogs develop into mature
pulmonary distomas and begin to lay eggs in about 90 days.

9. In the final host the parasites are taken into the alimentary
canal as encysted cercariae. They liberate themselves from the
cysts in the intestine and bore through the jejunum into the abdomi-
nal cavity. They then pierce the diaphragm, enter the thoracic
cavity, and piercing the pleura reach the lungs. In the parenchyma
of the lungs they form cysts and develop into adult forms.
10. The chief causes of pulmonary distomiasis are the eating of raw or insufficiently cooked crabs infected with the cercariae of *Paragonimus westermanni*, and the drinking of river water containing them.

In conclusion the author wishes to express his indebtedness to Professor Takaki, Chief of the Scientific Research Institute of the Taiwan Government, and others who have given him valuable assistance.

**BIBLIOGRAPHY.**

4. Matsuo, M., and Yokokawa, S., Results of the statistical observations on the visceral parasites among the natives of Formosa, *Taiwan Igakkwai Zasshi*, 1912, No. 114.
12. Yoshida, S., On the intermediate host of the pulmonary distoma that occurs in the Prefectures of Osaka and Tokushima, Osaka Igakkwai Zasshi, 1915, xix, No. 9; On the intermediate host of the pulmonary distoma that occurs in the Prefecture of Okayama, ibid., 1915, xix, No. 10.
15. Yamagiwa, K., Lectures on general pathology, Tokyo, 1909, ii.

EXPLANATION OF PLATES.

PLATE 22.

Early developmental stages of *Paragonimus westermanni*.

Fig. 1. Eggs in fresh sputum. Zeiss oc. 2, obj. 45, oil immersion.

Figs. 2 to 4. Eggs in various stages of development. Zeiss oc. 2, obj. 45, oil immersion.

Fig. 5. Free swimming miracidia. Zeiss oc. 2, obj. 45, oil immersion.

Figs. 6 to 8. Sporocysts in *Melania libertina*. Zeiss oc. 2, obj. 45, oil immersion.

Fig. 9. Cercaria developed in *Melania*. Zeiss oc. 2, obj. 45, oil immersion.

Figs. 10 to 14. The youngest cercariae that lie in the liver of the fresh water crab, *Potamon obtusipes*. Zeiss oc. 2, obj. AA.

Figs. 15 to 18. Encysted young cercariae in the liver of a crab. Zeiss oc. 2, obj. AA.

Fig. 19. Full grown encysted cercaria. Zeiss oc. 2, obj. AA.

PLATE 23.

Fig. 20. Fresh water univalves, the first intermediate host of *Paragonimus westermanni*. Natural size. a, *Melania libertina* Gould; b, *Melania obliquegranosa* Smith.

Fig. 21. Fresh water crab, *Potamon obtusipes* Stimpson, the second intermediate host of *Paragonimus westermanni*. Natural size.

Fig. 22. Fresh water crab, *Potamon dehaanii* White, the second intermediate host of *Paragonimus westermanni*. Natural size.

PLATE 24.

The second intermediate hosts of *Paragonimus westermanni*.

Fig. 23. *Potamon sinensis* Milne-Edwards. Natural size.

Fig. 24. *Sesarma dehaanii* Milne-Edwards. Natural size.

Fig. 25. *Eriocheir japonicus* De Haan. Natural size.
PLATE 25.

Fig. 26. Jejunum of a kitten experimentally infected by *Paragonimus westermani*. Natural size. *a*, petechiae; *b*, mesentery.

Fig. 27. Omentum of the same film to show the worm attached on the surface. Natural size. *a*, young worm; *b*, stomach.

PLATE 26.

Fig. 28. Diaphragm of a kitten that had been experimentally infected by *Paragonimus westermani*. Natural size. *a*, young worm just piercing through the muscular layer; *b*, petechiae produced by the worm; *c*, tendinous region of the diaphragm.

Fig. 29. Liver of the animal shown in Fig. 28. Natural size. The brown irregular lines indicate the path of the young worm.

PLATE 27.

Fig. 30. Intercostal muscle of a kitten that had been experimentally infected by *Paragonimus westermani*. Natural size. *a*, ribs; *b*, intercostal muscle; *c*, young worm.

Fig. 31. Lungs of a pup experimentally infected by *Paragonimus westermani*. The specimen was examined a few days after feeding. Natural size. *a*, petechiae.

Fig. 32. Lungs of a pup experimentally infected by *Paragonimus westermani*, 50 days after feeding. Several cysts are present. Natural size. *a*, cysts.

PLATE 28.

Fig. 33. Section of the liver of *Melania libertina* that harbors the cercariae. *a*, liver parenchyma; *b*, cercariae. Zeiss oc. 2, obj. DD.

Fig. 34. Section of the gills of *Potamon obtusipes*, infected by encysted cercariae. *a*, encysted cercariae. Zeiss oc. 2, obj. AA.

PLATE 29.

Fig. 35. Section of the jejunum of a kitten experimentally infected. *a*, mucous membrane; *b*, connective tissue; *c*, internal muscular layer; *d*, external muscular layer; *e*, young distoma piercing through the intestinal wall; *f*, worm track. Zeiss oc. 2, obj. AA.

Fig. 36. Section of the diaphragm of a kitten experimentally infected. *a*, young worm in the muscle of the diaphragm. Zeiss oc. 2, obj. AA.

PLATE 30.

Fig. 37. Section of the liver of a kitten experimentally infected, showing the hemorrhagic spots caused by the young worm. *a*, hemorrhagic spots. Zeiss oc. 2, obj. AA.

Fig. 38. Section of the lung of a pup experimentally infected; 60 days after feeding. *a*, half grown worm. Zeiss oc. 2, obj. AA.
Plate 31.

Various developmental stages of *Paragonimus westermanni* in the final host.

Fig. 39. Young worm, 3 days after feeding. × 30.

Fig. 40. Young worm, 14 days after feeding. × 30.

Fig. 41. Young worm, 21 days after feeding. × 30.

Fig. 42. Young worm, 25 days after feeding. × 30.

Fig. 43. Half grown worm, 50 days after feeding. × 15.

Fig. 44. Mature worm 90 days after feeding. × 15.
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