**Paragonimiasis in Korea**

—Biological Aspect—

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**BIOLOGICAL ASPECTS**

The lung fluke is one of the trematoda which belongs to the Genus Paragonimus. Though several species of human and animal strains have been described by many workers in various parts of the world, *Paragonimus westermani* (Kerbert, 1878) Braun, 1899 is the one species only known in Korea.

Kobayashi (1918~1919) studied the morphology of immature and adult lung flukes from a variety of both natural and experimental hosts in Korea, and considered that the specimens from all these hosts, including man, belonged to the same species.

**Morphology**

**Adult**: The reddish-brown living worm has an indefinite shape owing to its constant expansion and contraction; while completely contracted, it is spherical. The preserved parasite resembles a coffee bean and is greyish, with an abruptly rounded anterior and a somewhat tapering posterior end.

Mature adults range from 7 to 12 mm in length, from 4 to 7 mm in breadth and from 3.5 to 6 mm in thickness. Kobayashi (1917, 1918, 1919) studied the integument of immature and adult lung flukes, and found that the cuticular spines were generally chisel-shaped, but showed variations from needle-shaped to broad scale-like spines with serrated edges differing in size but averaging 31 by 14 μ. He also reported that the spines of 24-day-old immature adults showed less variation than those of older specimens. These spines were quite uniformly needle-shaped and tapered terminally to a sharp point. In transverse section near their base, they were ellipsoidal or even circular; toward the tip they were gradually more flattened, having a lancet shape. Usually the tip was sharp, but a few were truncated. The spines were placed singly and arranged in diagonal rows, and differed from the spines in older specimens which were frequently chisel-shaped, with the apex usually notched in the middle and often serrated.

The ventral sucker, 0.08 cm in diameter, situated in the mid-line just anterior to the equatorial plane of the body, is often completely invaginated, and the oral sucker is of equal size. The ovary is on the left or right side just back of the ventral sucker. The uterus is on the other side and extends laterally further toward the edge of the worm than does the ovary. The testes develop on each side of the body back of the ovary and uterus. The digestive system is characteristic in having a very short esophagus and long undulating ceca, showing three windings which reach to the posterior end of the body. The excretory bladder is a large tube, flattened laterally; it extends from the posterior end of the body forward almost to the bifurcation of the intestinal ceca. Kobayashi (1919) found that in full-grown specimens the excretory bladder is much flattened laterally. In an adult 8.0 by 3.0 by 3.0 mm, it had a length of 5.5 mm, a dorsoventral diameter of 1.4 mm, and a width of 0.7 mm. In an immature specimen, he also found that on each side there were five secondary collecting tubules each with
three capillaries connected with the anterior collecting tube and that the same number connected with the posterior collecting tube, making 10 groups of three capillaries on each side or a total of 60 capillaries. The formula for the excretory system was $2(5 \times 3) + (5 \times 3) = 60$. The vitellaria which are widely distributed on both ventral and dorsal surfaces of the body have four main vitelline ducts, two of which arise from the anterior part of the worm and two from the posterior. These join the transverse vitelline ducts which are located just back of the ovary and uterus. The genital atrium is a pear-shaped cavity that receives the male and female ducts. It has a length of 0.45 mm and opens to the outside in the genital pore, which is located just back and to the side of the ovary.

Egg: The egg of the lung fluke is yellowish-brown in color and is thick-shelled. The average size of the egg is 85 by 53 μ and varies from 73 to 118 μ in length and from 48 to 67 μ in breadth. It is operculated with the operculum more or less distinctly thicker than the rest of the shell and is frequently asymmetrical. At oviposition, the ovum is in the single-celled stage and is surrounded by five to ten coarsely granular yolk cells, which are polygonal in shape with a diameter of about 0.03 mm. They are coarsely granular, especially near their periphery, and their nuclei measure about 0.005 mm in diameter (Yokogawa et al. 1963).

Miracidium: During the early stages of development of the miracidium, the yolk cells gradually dissolve, beginning with the parts closest to the fertilized ovum. By the end of one week, their coarse granules and nuclei begin to disappear. Soon most of the yolk granules from these cells are dissolved, to serve as food for the developing embryo (Watanabe 1935). The fully developed miracidium of the paragonimus has a size of about 0.08 by 0.04 mm. It is covered with four rows of ciliated ectodermal plates. Those of the first row, six in number, are triangular; six in the second row are rectangular; the three in the third row are also rectangular, and there is a more or less triangular plate at the posterior end of the body.

At the anterior tip of the miracidium, at the point of the so-called rudimentary digestive gland, is a small slightly protrusable papilla. Two lateral projections are present between the first and second row of plates. The so-called rudimentary digestive sac, which appears to be composed of four cells, since four nuclei can be made out in it, extends back to the anterior margin of the second row of plates. Back of it is the central nerve mass. Two flame cells are present at about the middle of the body, which have very convoluted tubules that open on each side in the spaces between the second and third row of plates. The entire body except at the anterior tip and in the spaces between the epidermal cells, is covered with cilia that are about 10 μ in length. Several germinal cells are present in a tightly-packed group in the body cavity in the posterior half of the body of the miracidium.

The vitelline membrane bulges through the opercular opening before it is ruptured by the miracidium. The free-swimming miracidium, 80 by 40 μ, has 16 ciliated epidermal cells arranged in four rows. It cannot survive over 24 hours at 25°C unless it penetrates the head or mantle of a snail, but remains active for three days at 7°C.

Sporocyst, Redia, Cercaria, Metacercaria: The miracidium loses its ciliated epithelium either at the time of penetration or within the snail. Within 20–30 days it becomes first an ellipsoidal and later an elongated sacculated sporocyst 400 by 160 μ, which contains 20 to 30 rediae. The mother sporocysts are found free in the lymphatic system in practically every part of the snail, especially along the esophagus, stomach and intestine. The first-generation rediae, after escaping from the sporocyst as early as 26 days after infection, develop in the lymph sinuses near the digestive tract and liver. They are short and truncated with an invaginated posterior end, prominent collar germinal cells, and with a digestive tract consisting of a pharynx, a short esophagus and an elongated intestine. Ameel (1651) found first-generation rediae to contain well-developed second-generation rediae 63 to 70 days after infection. The average size is 0.293 by 0.133 mm. Second generation rediae vary in length from 0.851 to 1.350 mm and in width from 0.249 to 0.352 mm.
The pharynx is small in relation to the total size, measuring about 0.072 mm in diameter. The intestine is large and extends for about two-thirds the length of the body. The excretory pores are back of the middle of the body; from each of them a main collecting tube runs forward. It divides into short anterior and posterior collecting tubes which usually receive the capillaries from four flame cells. Generally they are larger and have sloping, rounded extremities, a birth pore and no collar. These daughter rediae produce cercariae. It is estimated that a mother sporocyst can produce at least 25 first-generation rediae and that each of these can produce at least 30 daughter rediae.

The cercaria of Paragonimus westermani, 225 by 80μ in average, belongs to the microcercous type with a very short cylindrical tail, 19 by 13μ. The body is covered with spines. The round or slightly elongate, terminal oral sucker carries on its anterodorsal surface a simple, boring stylet. The small oval ventral sucker lies slightly posterior to the middle of the body above the muscular, expansile, trigonate excretory bladder. The main collecting tubes on each side form a convoluted mass extending up to about the level of the middle of the ventral sucker, where they receive the anterior and posterior collecting tubules. These collecting tubules each receive the capillaries from five groups of three flame cells each, making the flame cell formula 2（3+3+3+3+3）+(3+3+3+3+3)=60.

The digestive tract consists of a slender prepharynx, a small pharynx, a short esophagus, and distinct ceca that extend about half the body length. The genital cells lie between the ventral sucker and excretory bladder. There are eight lateral and six smaller median penetration glands with ducts opening anteriorly near the stylet. Kobayashi (1921) described, in addition to the penetration glands, two irregular rows of gland cells on each side of the body. Unless cercariae penetrate the articulations of a crustacean host, they perish in 24 to 48 hours at 22°C.

Kobayashi (1917, 1918) and several other workers reported that cercariae of Paragonimus westermani, after entering the crab or cray fish, lose their tails in about 4-7 days, and after that are surrounded by a thin membrane that become attached to the host tissue. Gradually, the inner cyst wall is laid down, first as a thin layer, and finally as a thick rigid cyst wall consisting of two layers. The average size is 350-480 x 330-480 μ. The metacercaria inside of the cyst wall gradually increases in size, and its digestive system becomes completely developed. The excretory bladder elongates and become crowded with concretions. Their complete development is accomplished in 42-54 days in summer, while in the autumn with cooler temperature it takes 96 to 106 days (R. Ando, 1920). The conspicuous features of the mature encysted metacercaria are the large median excretory bladder filled with highly refractile excretory granules and the twisted lateral intestinal area. Pigment present in the parenchyma of the metacercaria gives it a pinkish cast, recognizable to the naked eye.

**Hosts**

Definitive Host: Though paragonimiasis (the local name is To-Zii) has been recognized for many years in Korea, the actual infection was reported in the first quarter of the 20th century (Ko, 1917; Mori, 1915; Kagami, 1916; Hara, 1924).

As is well known, the parasite has a very wide distribution in domesticated and wild mammals, which feed on crabs and cray fish. Several animals were reported as hosts in Korea.

Kawamura (1916) fed the metacercariae to dogs, cows, hogs and hens, and found that dogs, hogs, cows and rabbits were infected easily, while the domestic fowl was not infected as it might be expected. However, hogs do not consume the crustacean host, so it is presumed that infection in dog is present in the ingestion of contaminated food or drinking water. Soh (1958) found paragonimus eggs from the stool of a tiger at the Seoul Zoo. In regard to wild animals the tiger, cat and weasel, etc. will be infected whenever it consumes infected crustacean.

The First Intermediate Host: Semisulcospira libertina (Gould) is the most important species which serve as the intermediate host in Korea among Thiaridae (Melanidae), though there are several
varieties: S. libertinia extensa (Von Martens); S. libertinia multincinta; Melania amurensis Gerstfeld, 1889; M. gottscheli MTS, 1886; M. nodiperda MTS, 1894; M. nodiperda var. quinaira; M. paucincinta MTS, 1894 were listed as a probable intermediate host by Kobayashi (1921, 1925). The adult shell of the Semi- sulcospira libertinia varies in length from three-fourths of an inch to two inches. It is somewhat spindle-shaped, with slightly flattened whorls (Yokogawa, etal 1960). The length of the aperture is equal to, or slightly less than half the total length of the shell in unornamented specimens. The spiral sculpturing consists of many small raised threads which are generally more prominent on the base of the shell. Axial sculpturing when present is in the form of wrinkles. Short ribs are set just below the suture. Some specimens are almost entirely smooth. The color of the shell varies in individuals from dark brown to light yellowish brown, which is sometimes flushed with a greenish blue. Juveniles and some adults occasionally have three or four spiral streaks of dark brown in the shell. Melanita amurensis (Hua amurensis) has a solid shell from one-half to one inch in length, and usually has a dark brown color.

Second Intermediate Hosts: As in other districts, crabs and crayfish are the known second intermediate host of Paragonimus westermani in Korea (Kobayashi 1917, 1919). Eriocheir sinensis H. Milne-Edwards,.....Moriyasu (1915) found the metacercariae of Paragonimus westermani at Kangwha island for the first time, and Kagami (1916), Miyairi (1916) also found them in Hamkyung-Namdo. Probably this species may be the main intermediate host among crabs in Korea. The preferred habitat of this crab is described by Kobayashi (1925) is the rice field and the larger streams in the low lands. Kobayashi (1918) previously reported that the cysts in the crabs were most frequent in the gills and in the muscles of the proximal part of the ambulatory legs.

Cambaroides similis (Koebele)....Miyairi (1916) was the first who found the metacercaria of P. westermani from this crayfish. This species is called "Ga-Zue" in Korea and is very common in mountainous streams. The cysts are most numerous in the muscles or the liver of the cephalothorax. The gills and muscles of the appendages also contained cysts, but in small numbers. Kobayashi (1918) found 1,016 metacercariae in one crayfish in an endemic area. Though there are several other species of crab and crayfish in Korea, yet there have been no definite reports that they serve as the intermediate host of Paragonimus westermani.

Life Cycle

Clean water is the suitable medium for the development of paragonimus eggs. At 20~30°C in shaded areas, the egg cell develops into the miracidium within two weeks, then hatch in from one to six weeks. The hatched larvae survive for 12~24 hours at 20~25°C, but may remain viable for about 3 days at 7°C. They can swim as far as 7.5 mm in 2.5 seconds (Chen, 1940).

During the act of penetrating the snail intermediate host, the miracidia shed their ciliated plate. As soon as the naked miracidium reaches a lymph space, it begins to develop into a mother sporocyst. In order to determine what part of the body was most frequently penetrated, Yokogawa and Ito (1960) exposed a snail to very large numbers of miracidia at a temperature of 30°C for five hours and found 86 in the tentacles, 50 in the lips, 39 in the head, 23 on the dorsal side of the foot, 206 on the ventral side of the foot, 91 in the body and 181 in the anterior part of the mantle. After the miracidium enters a suitable species of snail, it develops successively into a sporocyst, mother rediae, daughter rediae and cercariae.

The cercariae that emerge from a snail about 13 weeks after infection travel with a leech-like motion. Actually they cannot swim, but when the water is agitated, they may release their hold and float along in the current. Kruidenier (1963) observed that the mucoid glands discharge their secretion during the final stages of the development of the cercariae after they have escaped from the rediae into the tissues of the snail. Cercariae at room temperatures live outside the host for from one to two days, while at 7°C they may live a day or more.

There are two reports concerning the mode of infection by cercariae of the second intermediate host. Wu (1935) observed the cercariae of P.
westernani penetrating the joints of the legs of crabs. He was able to obtain experimental infection of crabs placing them in dishes with free cercariae. On the other hand, Yokogawa (1922) reports that the second intermediate hosts can be infected by eating snails harboring mature cercariae. He found a considerable number of cercariae within the intestinal wall and the blood vessels of the gills of the Eriocheir japonicus in one endemic area. Cercariae after entering crabs or crayfish lose their tails in about 4 to 7 days, and then are surrounded by a thin membrane that becomes attached to the host tissue. Kobayashi (1918) thought that it was formed by the tissue reaction of the host. Somewhat later, the inner cyst wall is laid down, first as a thin layer and finally as a thick, rigid cyst wall consisting of two layers. The complete development of the metacercariae is accomplished in 42 to 54 days in summer, while in the autumn, with cooler temperatures, it takes 96 to 106 days (A. Ando, 1920).

When the definitive host ingests the metacercariae, either within a second intermediate host or free, the excystment begins to take place soon after the cysts have passed from the stomach to the intestine (Yokogawa, 1918, 1919). After the excystment, the metacercariae penetrate the intestinal wall and enter the abdominal cavity. The penetration site of the larvae is from the beginning of the duodenum to within 8 cm of the cecum. Thence they migrate up to the diaphragm and pleural cavity and enter the lungs through their surfaces. Recently Yokogawa (1920) observed the young worm in the abdominal cavity penetrate into the muscle of the abdominal wall and develop for 5-7 days before traveling to the lung or other parts of the body.

Besides the usual route of lung infection, ectopic infection of P. westernani has been reported frequently in endemic area. Soh et al (1962) examined the distribution of P. westernani in experimental dogs. Six dogs were examined 45-86 days after the feeding of metacercariae of P. westernani; 15.7% of the worms were still in the abdominal cavity and organs; 84% of the worms were found in the various thoracic organs, including the pleural cavity. Only 47% of them were in the lung, and only two worms were detected in the archnoid tissue of the vertebra in one dog. Neurorsurgical aspects will be discussed in a subsequent article.

In contrast to the animal, in human infections, usually one parasite is found in a cyst, although Muta (1911) reported finding three worms in a cyst at autopsy of a Korean.

The Development of P. westernani in man has not been followed in detail. Eggs first appear in the sputum about two and one half to three months after infection, while worms developing in abnormal situations take much longer to mature.

Concerning the life span in the definitive host, there have been several reports. The longest period was 20 years (O. Ando, 1922). Taniguchi (1893) reported a case in which a living fluke was extracted from an orbital tumor in a woman which had been present for over 15 years. From several reports, it may be presumed that the worm can survive around ten years in a host.

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