The Role of the Parasite Life Cycle in Pathogenesis of Infectious Diseases

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Abstract - Indonesia is a developing country that has various risk factors that can cause parasitic infections to develop. The role of the life cycle of worms and other parasites has been widely studied before. However, there is still little review of its pathogenesis in Indonesia. The purpose of this article is to examine the role of the parasite life cycle in the pathogenesis of infectious diseases. Based on this review, it can be concluded that Diphyllobothrium latum, Taenia solium, Echinococcus granulosus, Hymenolepis nana, Dypilidium caninum, Schistosoma japonicum, Fasciolopsis buski, Heterophyes, Echinostoma, Clonorchis sinensis, Fasciola hepatica, Dicrocoelium, Paragonimus westermani, trichiura, Necator americanus, Ankylostoma duodenale, Strongyloides stercoralis, Trichinella spiralis, Angiostrongylus cantonensis, and Wuchereria bancrofti have different life cycles. This difference will have an impact on the different pathogenesis for each infection. Enforcement and treatment also differ based on the underlying pathogenesis.

Keywords – life cycle, parasite, pathogenesis, infectious disease

INTRODUCTION

Indonesia is a developing country that has various risk factors that can cause Soil Transmitted Helminth (STH) infections to develop, such as a humid tropical climate, poor personal hygiene and sanitation, low education and socioeconomic levels, high population density and poor living habits not good. According to WHO, it is estimated that there are 1.2 billion people infected with A. lumbricoides, 795 million people with T. trichiura infection and 740 million people with hookworm infection. It is estimated that more than two billion people are infected with worms worldwide, about 300 million people suffer from severe helminth infections, and about 150,000 of them die from STH infections. According to the World Bank report, the highest prevalence of helminthiasis can be found among primary school age groups aged 5-14 years. Worms can also occur in the age range of up to 20-25 years, especially those caused by hookworms. [1]

The role of the life cycle of worms and other parasites has been widely studied before. However, there is still little review of its pathogenesis in Indonesia. The purpose of this article is to examine the role of the parasite life cycle in the pathogenesis of infectious diseases. A good understanding of the pathogenesis will certainly lead to the establishment of the right diagnosis.

RESULT AND DISCUSSION

Diphyllobothrium latum

In its life cycle, Diphyllobothrium latum involves one definitive host and two intermediate hosts. Humans, dogs or cats are the definitive hosts for this worm. Adult worms can live up to 13 years in the human small intestine. The first intermediate host in the life cycle of this worm is cyclops (cyclops, diaptomus) which belongs to the crustacean group, while fish act as the second intermediate host. Together with the feces of patients with worm eggs in the intestines, they will be...
removed from the body of the host. Eggs that enter the water will hatch into coracidium larvae (coracidium), which will then swim freely in the water. Coracidium eaten by cyclops, within 3 weeks in the body of the cyclops coracidium turns into procercoid larvae (procercoid). In the body of the fish (second intermediate host) that eats cyclops within 3 weeks the procercoid larvae will turn into plerocercoid larvae (plerocercoid) which are infective for the definitive host (human, dog or cat). Plerocercoid will develop into adult worms in the intestine of the definitive host. [2]

_Echinococcus granulosus_ is a zoonotic parasite, which can be transmitted from pigs to humans and vice versa, humans act as definitive hosts for adult worms to live, while worm larvae (cysticercus cellulosae) are found in the form of cysts in the tissues and organs of pigs that act as intermediate hosts. Adult worms release the most end gravid segments in the form of chains, which break in the intestine so that worm eggs can be found in the patient's feces. Worm eggs that are released from the human body with feces if eaten by pigs, in the intestines of pigs the egg wall will break, and the oncosphere will be released. Because it has hooks, the oncosphere can penetrate the intestinal wall and enter the bloodstream. The oncosphere will spread to the tissues and organs of the pig's body, especially the tongue, neck, heart and locomotor muscles. Within 60-70 days after infection, the oncosphere will turn into cysticercus cellulosae (cysticercus cellulosae) larvae. Infection in humans occurs from eating raw or undercooked pork, which contains cysticercus larvae. In the human intestine, the scolex will exvaginate and attach itself with a suction device to the intestinal wall. The scolex then grows into an adult worm and then forms a strobila. Within 2-3 months the worms have grown into adult worms that have been able to produce eggs to continue their life cycle. [3]

**Hymenolepis nana**
The natural definitive hosts for this worm are humans, mice and mice. There is no need for an intermediate host to complete its life cycle. Infective worm eggs that are ingested will hatch in the small intestine, then the larvae will penetrate the walls of the intestinal villi. Within 4 days the larvae will develop into cysticercoids. Cysticercoid will penetrate outside the intestinal villi, enter the lumen of the intestine and then attach to the intestinal mucosa and grow to develop into adult worms within 10 to 12 days. Worm eggs can be found in the patient’s feces within 30 days of infection. In the intestines of patients with eggs that are in the feces can hatch so that it will cause a repetition of the cycle. This condition is known as internal autoinfection [5].

**Dipylidium caninum**
The natural definitive hosts for this worm are dogs, cats and other carnivores. Sometimes humans can act as definitive hosts. As intermediate hosts in the life cycle of
*Dipylidium caninum* are the dog flea, cat flea and dog tuma (*Trichodectes canis*). After the worm eggs are eaten by flea larvae or other intermediate hosts, the oncosphere will emerge from the envelope, penetrate the intestinal wall and grow into infective cysticercoid larvae. If adult fleas derived from flea larvae containing cysticercoid larvae are eaten by the definitive host, in about 20 days the cysticercoid will grow and develop into adult worms. *Dipylidiasis caninum* has been reported to infect children under 8 years of age, especially children under 6 months of age. The way of infection is orally, which is swallowed by fleas or infective dog and cat fleas with food and drink or infected directly from hands contaminated with feces of sick dogs and cats [6].

*Schistosoma japonicum*

Various types of mammals including humans can act as definitive hosts for Trematode worms. Trematode worm life cycle requires an intermediate host, namely mollusks that live in fresh water such as snails and snails. Some species of Trematode worms require a second intermediate host such as fish, crabs, aquatic plants or ants. In the body of the definitive host live adult worms that carry out the reproductive process. Female worms produce eggs that will be excreted with the patient's feces or urine. If the eggs enter the water, the eggs will hatch into miracidium larvae (miracidium). To be able to continue its life cycle, miracidium larvae must be able to enter the snail's body, which will then develop into sporocysts (sporocysts) which will then grow into redia, then become cercariae larva (cercaria). Cercariae leave the snail's body and swim freely in the water or grow first to become metacercariae (metacercaria) before entering the human body or other definitive host and developing into adult worms. In humans, Trematode infection can occur in various ways. In *Schistosoma*, the infective stage of this worm is the cercariae which enter the body of the definitive host actively by penetrating the unprotected skin while in the water [7].

*Fasciolopsis buski*

Acting as the definitive hosts for these worms are humans and pigs. Freshwater snails of the genus Segmentina, Hippeutis, or Gyraulus are intermediate hosts in the life cycle of this worm. Trematodes in their life cycle require a second intermediate host, namely aquatic plants which are the place for the development of infective larvae (metacercaria). Human infection occurs when humans are ingested by infective larvae (metacercaria) found in aquatic plants. In the duodenum, the larvae will separate from the plant tissue, attach themselves to the mucosa of the small intestine and then develop into adult worms. Within 25 to 30 days, adult worms are able to produce worm eggs. Adult worms generally live in the human intestine for less than 6 months. If the worm eggs that come out with the patient's feces enter the water, then within 3 to 7 weeks at a water temperature of about 300 Celsius, the eggs will hatch into miracidium larvae that can swim in the water. Within 2 hours the miracidium should be able to enter the body of the snail which is the first intermediate host. The larvae will die if within 5 hours after leaving the patient's body they cannot enter the snail's body [8].

*Heterophyes*

The definitive hosts for this worm are humans and fish-eating animals, while freshwater snails, such as Pirenella and Cerithidea, are the first intermediate hosts. As the second intermediate host are several types of fish, for example Mugil, Tilapia and Acanthogobius. Worm eggs that enter the water when eaten by snails, in the snail's body the eggs hatch and the miracidium larvae will grow into sporocysts, then redia and then develop into cercariae. The cercariae will then exit the snail's body. and look for fish that act as intermediate second hosts. Under the scales of fish or in the flesh of cercariae will grow into metacercarial cysts which are infective for the definitive host. Infection in humans occurs due to eating raw fish containing the infective stage of this worm (metacercaria) or eating undercooked infective fish. Within 2 weeks after infection, the larvae have developed into adult worms that are capable of laying eggs. Heterophyes are parasites on humans and a wide variety of animals such as cats, dogs and fish-eating mammals or birds. Fishermen who suffer from heterophiasis are a source of infection for other residents, because they generally defecate in the waters where they earn a living [9].

*Echinostoma*

Worm eggs that fall into the water within a few weeks will hatch. The miracidium larvae will
come out, enter the water and then swim to find small snails that become their first intermediate hosts, such as Gyraulus and Anisus. Inside the snail's body, the miracidium will soon develop into the parent redia, redia and then cercariae. The cercariae larvae immediately leave the body of the snail which is the first intermediate host, then enter the water to find the second intermediate host, namely the large snail, namely Pila and Corbicula. In the body of the second intermediate host, the cercariae will develop into metacercariae which is an infective stage for the definitive host. Freshwater fish and aquatic plants may also act as second intermediate hosts [10].

**Clonorchis sinensis**

If the eggs that come out with the patient's feces enter the water, in the water the eggs will hatch into miracidium larvae. In the body of water snails (Bulinus, Semisulcospira, or Hua) that eat them, the larvae of miracidium then develop into sporocysts, which then develop into redia and finally cercariae. After that, the cercariae leave the snail's body which is the first intermediate host, then look for a second intermediate host, namely freshwater fish (Cyprinidae). The cercariae penetrate the underside of the fish scales and grow into metacercariae, which then develop into metacercarial cysts which are infective for the definitive host [11].

**Fasciola hepatica**

The definitive hosts for this worm are humans and herbivores, while the freshwater snail Lymnea acts as the main intermediate host. The second intermediate host is aquatic plants or grass, which is a place for the development of metacercarial cysts, which are the infective stage of this worm. If the worm eggs that come out with the patient's feces into the water, within 9 to 15 days in the eggs there will be growth of miracidium. After hatching, the miracidium will swim to find the snail which is the first intermediate host. In the snail's body, miracidium grows into sporocysts, redia, and then develops into cercariae (cercaria). The cercariae will come out of the snail's body and swim in search of aquatic plants or grass and turn into infective metacercariae cysts. If humans are ingested in the infective stage (metacercarial cysts) found in aquatic plants, in the duodenum the metacercariae will separate from the aquatic plant tissue, migrate through the intestinal wall and reach the liver via the bloodstream. Most of the metacercariae will reach the bile ducts and gallbladder, then will develop into adult worms [12].

**Dicrocoelium dendriticum**

The main definitive host for *Dicrocoelium dendriticum* is sheep, while humans are rarely infected with this worm. The first intermediate host for this worm is a land snail, such as Cochlicella and Abida, while the second intermediate host is the ant Formica fusca. If the eggs that come out with the patient's feces are eaten by land snails, the eggs will hatch into miracidia larvae in the snail's body. The miracidium larvae then turn into sporocysts, which then develop into cercariae. The cercariae that come out of the snail's body when eaten by ants will grow into infective metacercariae. When the ants are eaten by the definitive host, the metacercariae will exit the cyst, penetrate the intestinal wall of the definitive host and then go to the liver and bile ducts through the portal system [13].

**Paragonimus westermani**

Acting as the definitive host Paragonimus is an animal that eats crabs and humans. As the first intermediate host in the life cycle of this worm are snails of the genus Hua, Semisulcospira and Thiara, while crabs or stone prawns are the second intermediate host. Together with the patient's phlegm or feces, worm eggs come out of the definitive host's body. In the water the eggs will develop and then hatch into miracidium larvae within 3 weeks. Miracidium will then enter the snail's body and grow into sporocysts, then become redia and finally develop into cercariae. The cercariae larvae then leave the snail's body, enter the crab or crayfish body, and develop into infective metacercariae. Paragonimiasis occurs when people eat crabs or raw shrimp that contain metacercariae which are the infective stage. Metacercariae then develop into young worms in the duodenum, then penetrate the intestinal wall and enter the abdominal cavity. Then the young worms will penetrate the diaphragm, enter the pleural cavity and finally reach the lung tissue. Young worms grow into adult worms in the cyst cavity that forms near the bronchi [14].

**Ascaris lumbricoides**

Out with the patient's feces, fertilized worm eggs if they fall on moist soil and optimal
temperatures, the eggs will develop into infective eggs, which contain worm larvae. In humans, infection occurs with the entry of infective worm eggs with food or drink contaminated with soil containing feces of ascariasis sufferers. In the small intestine the upper part of the egg wall will break and then the larvae come out, penetrate the small intestine wall and enter the hepatic portal vein. With the flow of venous blood, the larvae circulate to the heart, lungs, then through the capillary walls into the alveoli. This larval migration period lasts about 15 days. After that, the worm larvae propagate to the bronchi, trachea and larynx, to then enter the pharynx, esophagus, then down to the stomach and finally to the small intestine. Then the larvae molt and grow into adult worms. The migration of worm larvae in the blood that reaches the lungs is called "lung migration". Two months after the entry of infective eggs through the mouth, female worms begin to be able to lay eggs. An adult *Ascaris lumbricoides* worm can lay eggs with the number of egg production reaching 200,000 eggs per day. [15]

**Enterobius vermicularis**

The only definitive host for this worm is humans. To complete the *Enterobius* life cycle, no intermediate host is required. In the perianal and perineal area of the patient, the eggs laid by female worms within 6 hours have grown into infective eggs because they contain worm larvae. Enterobiosis infection can occur in 3 ways, namely oral transmission, respiratory transmission and retrofection. Transmission occurs through the mouth if the infective eggs are carried from the patient's own hands to the mouth (autoinfection) or occur due to handling objects contaminated with infective eggs, such as bedding, pillows or the patient's underwear. Transmission through breathing, occurs because the infective eggs flying in the air are inhaled by the sufferer. Retroflective transmission is transmission that occurs because the worm larvae that hatch in the perianal area re-enter the patient's intestine, then develop into adult worms. The ease of transmission makes enterobiosis an infectious disease that often infects all family members, residents of orphanages or nursing homes, in dormitories, and in places where many people gather for a long time. After entering the mouth or through the airway due to inhaling polluted air, the worm eggs will enter the intestine and in the duodenum the eggs will hatch. The rhabditiform larvae that are formed will grow into adult worms in the jejunum and in the upper part of the ileum. It takes 2 to 8 weeks for this worm's life cycle to take place completely [16].

**Trichurus trichiura**

The eggs of this worm undergo maturation and become infective in the soil within 3-4 weeks. If humans are ingested eggs of infective worms, then in the small intestine the egg wall breaks and the larvae exit to the cecum and develop into adult worms. Within one month since the entry of the infective eggs into the mouth, the worms have become adults and the female worms have begun to be able to lay eggs. Adult *Trichurus trichiura* can live for several years in the human intestine [17].

**Hookworm**

The life cycle of *Ancylostoma duodenale* and *Necator americanus* only requires one type of definitive host, namely humans. No animal acts as a reservoir host. After leaving the patient's intestine, hookworm eggs that fall on the ground within two days will grow into rhabditiform larvae that are not infective because these larvae can live freely in the soil. After molting twice, the rhabditiform larvae within one week will develop into infective filariform larvae that cannot forage freely in the soil. To be able to develop further filariform larvae must find a definitive host, namely humans. The filariform larvae will infect human skin, penetrate the blood and lymph vessels and then enter the blood and follow the bloodstream to the heart and lungs. After the filariform larvae penetrate healthy human skin, they enter the blood and lymph vessels, circulate in the bloodstream, enter the right heart, and then enter the pulmonary capillaries. Then the filariform larvae penetrate the capillary walls into the alveoli. After molting twice, the worm larvae migrate to the bronchi, trachea, larynx and pharynx, finally being swallowed into the esophageal tract. In the lumen of the esophagus the larva molts for the third time. Migration of larvae lasts about ten days. From the esophagus the larvae enter the small intestine, molt a fourth time, then grow into male and female adult worms. Within a month, female worms can lay eggs to continue their offspring. [18]
Strongyloides stercoralis
The life cycle of Strongyloides stercoralis does not require an intermediate host. Adult worms live in the human intestine which acts as the definitive host, while some types of animals can act as reservoir hosts that become a source of transmission for humans. In the intestinal mucosa, worm eggs are released by the mother worm and soon hatch into rhabditiform larvae. These larvae will develop through three life cycle pathways:

1. Direct life cycle. Together with the feces of patients with rhabditiform larvae fall to the ground, growing into infective filariform larvae. Filariform larvae penetrate the host skin, undergo lung migration, and then develop into adult worms in the patient's intestine.

2. Indirect life cycle. The rhabditiform larvae, which fall on the ground with the patient's feces, develop directly into free-living adult worms. The adult worms then give birth to rhabditiform larvae which then develop into infective filariform larvae. Filariform larvae penetrate the host skin, followed by lung migration, then grow and develop into adult worms in the patient's intestine.

3. Autoinfection. The rhabditiform larvae present in the intestine turn into filariform larvae, which then penetrate the intestinal mucosa and develop into adult worms [19].

Trichinella spiralis
Trichinella spiralis adults and their larvae are found in the same host body, but to complete their life cycle, this worm requires two hosts of the same species or of different species. For example, the life cycle of Trichinella spiralis in forest rats, for example, requires only one type of host, namely rats because of the cannibalistic nature of rats that eat each other. In addition to humans, pigs and mice which are the definitive hosts for this worm. Trichinella spiralis worms can also live in the bodies of dogs, cats and bears. In the natural environment, the life cycle of this worm can take place between groups of animals that are cannibalistic, such as groups of rats. Pigs can also become infected with these worms by eating garbage containing the flesh of dead rats. Humans are commonly infected with Trichinella spiralis by eating raw pork that contains cysts of worm larvae or undercooked meat. When in the small intestine, the cyst wall bursts and the larvae are released, then enter the intestinal mucosa. Within two days the worm larvae will develop into adult worms. A female Trichinella spiralis can give birth to up to 1500 larvae which are released in the intestinal mucosa. Then the larvae enter the bloodstream and lymph, spread to various organs and other body parts, especially to the muscles of movement such as the tongue, diaphragm, eyes, larynx, biceps, stomach, deltoid and gastrocnemius muscles. The larvae are mainly dispersed into glycogen-poor muscles, forming cysts in the area and remaining infective for a long time. Between the sixth month to the ninth month began to occur calcification of the cyst [20].

Angiostrongylus cantonensis
Angiostrongylus cantonensis infection in humans occurs due to ingestion of infective larvae contained in mollusk meat (snails, snails) or eating meat from mollusk-eating animals such as crabs, fish, and shrimp that are not cooked properly. Infection in molluscs occurs as a result of eating worm larvae that are excreted with the feces of infected rodents, which are the definitive hosts for this parasite. Humans can also be contaminated by infective worm larvae through their fingers when processing mollusk meat before cooking or through fruits and vegetables contaminated with infective mollusk mucus. [21]

Wuchereria bancrofti
The worm Wuchereria bancrofti is not a zoonotic parasite and humans are the only definitive host for this worm. No animal acts as a reservoir for this worm host. Mosquito genera Culex, Aedes and Anopheles can act as vectors for transmitting filariasis bancrofti. The life cycle of Wuchereria bancrofti is generally nocturnal periodic, so that microfilariae are only found in peripheral blood at night. Filaria that live in the Pacific region have more microfilariae found during the day, although in smaller numbers can also be found at night (diurnal subperiodic). In Thailand, Wuchereria bancrofti microfilariae are subperiodic nocturnal, meaning that they are more commonly found in peripheral blood at night. After the microfilariae circulating in the patient's blood are inhaled by mosquitoes, within 10 to 20 days the larvae develop into the infective third-stage larval stage (L3). The third-stage larvae, about 1500 to 2000 microns in length and body width between 18 and 23 microns, can be found in the proboscis sheath
of the mosquito which is the intermediate vector. If this mosquito bites another human, it will transfer the L3 larvae which will then actively enter the groin, scrotum or abdominal lymph channels, and live there. Before developing into adult worms in the human body, microfilariae undergo two molts of skin. At the age of five to 18 months female adult worms are sexually mature and after copulation with male worms can begin to give birth to microfilariae, which immediately enter the peripheral blood circulation system [22].

**CONCLUSION**

Based on this review, it can be concluded that *Diphyllobothrium latum*, *Taenia solium*, *Echinococcus granulosus*, *Hymenolepis nana*, *Dypilidium caninum*, *Schistosoma japonicum*, *Fasciolopsis buski*, *Heterophyes*, *Echinostoma*, *Clonorchis sinensis*, *Fasciola hepatica*, *Dicrocoelium dendriticum*, *Paragonimus westermani*, *Trichiura*, *Necator americanus*, *Ancylostoma duodenale*, *Strongyloides stercoralis*, *Trichinella spiralis*, and *Angiostrongylus cantonensis* have different life cycles. This difference will have an impact on the different pathogenesis for each infection. Enforcement and treatment also differ based on the underlying pathogenesis.

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