# 8
# Angiostrongyliasis

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Animal life is a major source of food for many of the world's populations, and the preparation and the eating of the animals is highly variable. In some societies, animal meat may be cooked, smoked, pickled, fermented, or eaten raw. Unfortunately, there are often parasitic infections in the animals that are transmitted to humans, especially when animal products are eaten raw or poorly cooked. There are many of these zoonotic parasites, and one that is emerging and spreading throughout the world is the rat-lung worm, *Angiostrongylus cantonensis.* The helminth in the natural rodent hosts is not pathogenic, when only a few worms are involved; however, when humans acquire the parasite after eating the infected molluscan intermediate or paratenic host, angiostrongyliasis leading to eosinophilic meningitis may develop and cause severe illness.

## History

*Angiostrongylus cantonensis* is one of 20 metastrongyle nematodes that reside in the vascular system of animals. Species of *Angiostrongylus* have been reported from animals since 1886 when *A. vasorum* was found in the pulmonary vessels of dogs in Europe. Other species of the parasite have been reported over the years from Europe, Africa, North and South America, Australia, and the Asian-Pacific basin and is found in rodents, canines, felines, and insectivores (Table 8.1). At the present time only two species, *A. cantonensis* and *A. costarecensis,* have been found to cause disease in humans; however, two other species. *A. mackerrasae* and *A. malaysiensis* may have the potential of being pathogenic in humans (Prociv et al., 2000).

*Angiostrongylus cantonensis* was first reported as *Pulmonema cantonensis* found in the lung of rats in South China in 1933 (Chen, 1935). Matsumoto (1937) found it in rats on Taiwan, and Yokogawa (1937) described it as a new species, *Haemostrongylus ratti. Pulmonema* and *Haemostrongylus* were subsequently synonymized to *Angiostrongylus* by Dougherty (1946). Mackerras and Sanders (1955) described the life cycle of *A. cantonensis* in rats, but it was later determined that these authors actually worked with *A. mackerrasae* (Bhaibulaya, 1968, 1975).

TABLE 8.1. *Angiostrongylus* species.

| Parasite | Host | Geographic Areas |
|---|---|---|
| *A. vasorum* | Dogs | Europe, South America, Australia |
| *A. raillieti* | Crab eating dog | Brazil |
| *A. tateronae* | Jerboa | West Africa |
| *A. ondatrae* | Muskrat | Russia |
| *A. cantonensis* | Rats | Asia, Pacific |
| *A. ten* | Marten | Japan |
| *A. gubernaculatus* | Badger, skunk | United States |
| *A. blarini* | Shrew | United States |
| *A. soricis* | Shrew | Poland |
| *A. chabaudi* | Wildcat | Italy |
| *A. sciuri* | Squirrel | Turkey |
| *A. michiganensis* | Shrew | United States |
| *A. sandarasae* | Rodent | East Africa |
| *A. mackerrasae* | Rats | Australia |
| *A. dujardini* | Rodent | France |
| *A. schmidti* | Rice rat | United States |
| *A. malaysiensis* | Rats | Southeast Asia |
| *A. costaricensis* | Rats | Central and South America |
| *A. minutus* | Mole | Japan |
| *A. siamensis* | Rats | Thailand |

A high prevalence of eosinophilic meningitis in humans was reported from the Caroline Islands in the Pacific in 1948 (Bailey, 1948) and from Tahiti in 1960 (Franco et al., 1960). The first report of human infection with *A. cantonensis,* however, was reported by Nomura and Lin in 1945 (Beaver and Rosen, 1964) when 10 actively moving immature worms were recovered from the cerebrospinal fluid (CSF) of a 15-year-old boy from Taiwan. The importance of the parasitosis was not recognized internationally, however, until Rosen and coworkers (1961, 1962) reported the findings of the nematode in the brain of a man who died in Hawaii. At about the same time, Prommindaroj et al. (1962) reported finding the parasite in the eye of a Thai male, and Alicata (1962) reported *A. cantonensis* as a pathogen in humans. In subsequent years, the parasite has been reported in rodents, definitive hosts, molluscan intermediate hosts, paratenic hosts (frogs, crabs, prawn, planaria), and humans worldwide. In 1986, Ubelaker changed the name of the helminth to *Parastrongylus cantonensis*. This change, however, has yet to be generally accepted since the disease is recognized internationally as angiostrongyliasis.

## Parasite/Biology

The morphological features of *A. cantonensis* have been described by Alicata and Jindrak (1970) and Bhaibulaya (1979). The nematode has been classified as a member of the superfamily Metastrongyloidea, family Angiostrongylidae. The family members have filariform bodies that taper slightly at both ends. In *A. cantonensis*, there are three lips around the mouth, one dorsal with two

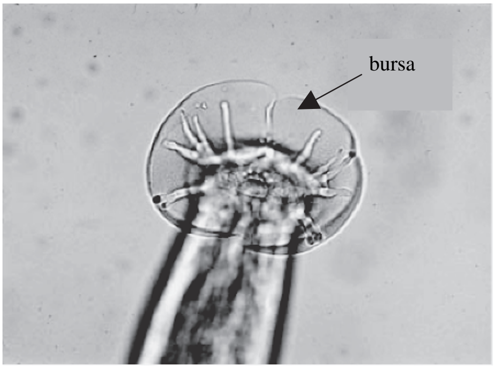


FIGURE 8.1. Posterior end of male *Angiostrongylus cantonensis* showing the bursa.

submedium papillae and two subventral lips each with two submedium papillae. The mouth opens directly into the esophagus followed by the intestine, which extends to the end of the body. The body is long and thin with a smooth transparent cuticle and transverse striae.

The males measure 20 to 25 mm in length and 0.32 to 0.42 in width. The caudal bursa of the male is small, well develop, kidney shaped, and single lobed (Fig. 8.1). The bursal rays have a ventral ray branched at a point two thirds of the length into a small ventroventral and a large lateroventral ray. Lateral rays arise from a common trunk; the anterolateral ray is thickened more than the others and projected like a thumb. The mediolateral ray and posterolateral ray usually originate from a common trunk. The posterolateral ray is normally shorter than the mediolateral ray and sometimes reduced to a stump. The external ray is simple and arises from between the lateral and dorsal rays. The dorsal is viable, emerging as a short trunk, terminating in several small digitations. Spicules are equal, slender, and with conspicuous striations (Fig. 8.2). The spicule measures 1.00 to 1.46 μm. A gubernaculum is present.

A female *A. cantonensis* has uterine tubules that wind spirally around a blood-filled intestine, which can be seen through the transparent cuticle as a barber's pole pattern. This is more apparent in the living parasite. A single thin-walled

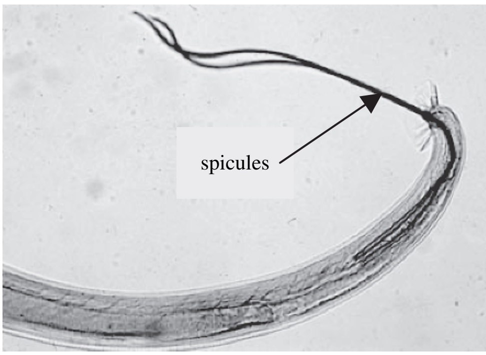


FIGURE 8.2. Posterior end of male *Angiostrongylus cantonensis* showing the bursa and extended copulatory spicules.

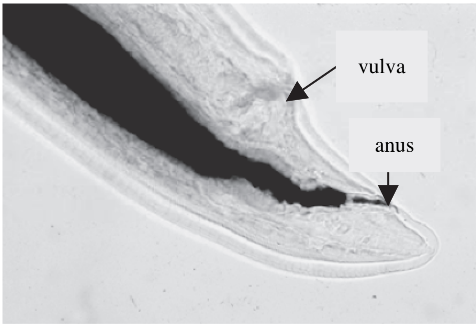


FIGURE 8.3. Posterior end of female *Angiostrongylus cantonensis* showing the vulva and anus.

vagina commences at the junction of the uterine tubules, extending posteriorly and opening at the vulva. The vulva and anus are close together near the posterior end of the worm. The anus is located about 0.05 mm and the vulva 0.2 mm from the tail end (Fig. 8.3). The females measure 22 to 34 mm in length and a maximum width of 0.34 to 0.56 mm (Fig. 8.4).

Adult male and female *A. cantonensis* live in the branches of the pulmonary artery of rats (Fig. 8.5). Following copulation, female worms deposite eggs that are carried by the blood to capillaries of the lung where they embryonate in 5 to 6 days (Fig. 8.6). The first stage larva hatches from the egg and breaks through the capillaries into the lung alveolus. The larvae subsequently migrate into the bronchioles up to the trachea, are swallowed, pass through the digestive tract, and out in the feces (Fig. 8.7). The first-stage larvae are eaten or penetrate the body of a molluscan intermediate hosts and migrate to the muscle tissue (Fig. 8.8). The larvae molt into second-stage larvae in 7 to 9 days and into the infective third-stage larvae (Fig. 8.9) in 12 to 16 days. Many species of the mollusks may serve as intermediate hosts, and when eaten by a rodent, the larvae are released from the molluscan tissue by digestion in the gastrointestinal tract. The released larvae penetrate the intestinal wall and are picked up in the blood and carried to the liver, heart, and lungs, and may reach the central nervous system in 1 to 2 days. The worms enter the neural parenchyma and molt into the fourth stage in 4 to 6 days.

FIGURE 8.4. Adult female *Angiostrongylus cantonensis* recovered from the pulmonary artery of a rat.

FIGURE 8.5. Section of adult *Angio-strongylus cantonensis* in the pulmonary artery of a rat.

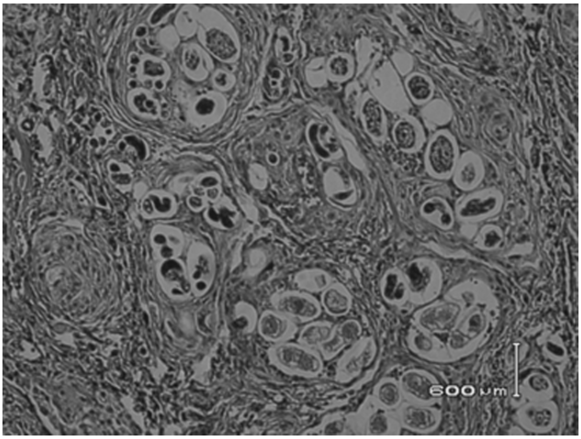


FIGURE 8.6. Section of a rat lung showing *Angiostrongylus cantonensis* eggs and larvae in the lung parenchyma.

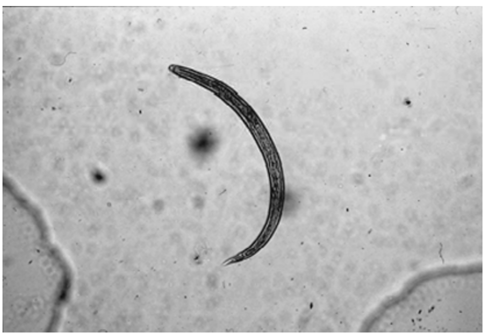

FIGURE 8.7. First stage larva of *Angiostrongylus cantonensis* recovered from an infected rat's feces.

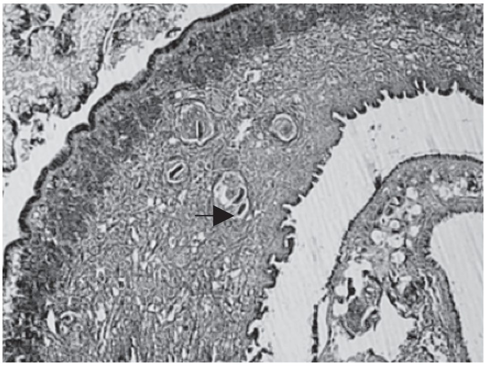

FIGURE 8.8. Developing larvae of *Angiostrongylus cantonensis* in snail muscle.

The final molt occurs in 7 to 9 days, and the young worms move into the subarachnoid space. They remain there for 10 to 14 days before invading the cerebral vein and migrate to the heart and lungs and eventually reach the pulmonary artery. Sexual maturity occurs in the artery and females deposit eggs. The eggs mature quickly and first-stage larvae (Fig. 8.7) may be found in the rat feces 6 to 7 weeks after the rat eats the molluscan intermediate host. The prepatent period is between 42 to 45 days in rats. The life cycle of the parasite is shown in Fig. 8.10.

## Geographic Distribution

*Angiostrongylus cantonensis* has been reported in rats and humans from most parts of the world (Alicata and Jindrak, 1970; Kliks and Palumbo, 1992; Prociv et al., 2000). It has been suggested that the parasite originated in Madagascar and was carried eastward to Asia by the giant African snail, *Achatina fulica*, a major intermediate host. It has also been suggested that the snail was introduced to some areas of Asia and the Pacific Basin by the Japanese military as a food source, and consequently it has been called the Japanese snail by some indigenous populations. Many Taiwanese in southern Taiwan eat the snail cooked and uncooked, and there are indications that the parasite can be picked up by simply handling the snail (Wan and Weng, 2004).

FIGURE 8.9. Third-stage larva of *Angiostrongylus cantonensis* digested out of snail muscle.

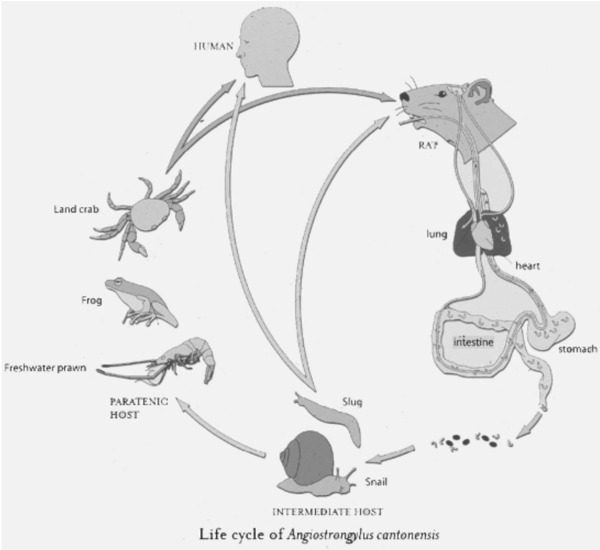


FIGURE 8.10. Life cycle of *Angiostrongylus cantonensis*. (From the Centers for Disease Control and Prevention.)

As indicated in Figure 8.11, the parasite today seems to be spreading from Asia and the Pacific Basin to the Western Hemisphere. Usually, once the parasite is found in rats and snails in an area, infections and eosinophilic meningitis eventually occur in humans.

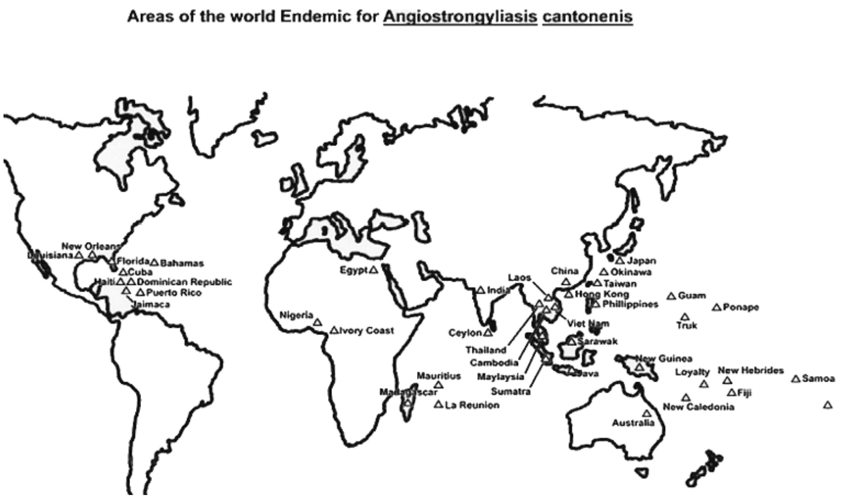


FIGURE 8.11. Map of the world indicating areas reporting *Angiostrongylus cantonensis.*

## Disease

The natural rat host will tolerate infection with *A. cantonensis* when less than 100 worms are involved; however, infection of more than 100 worms may lead to death of the animals. Rats and monkeys, on the other hand, may develop immunity to infection experimentally when given nonlethal immunizing doses of third-stage larvae (Heyneman and Lim, 1967; Cross, 1979). Monkeys were able to tolerate infections of hundreds or thousands of third-stage larvae after being given the immunizing infections (Cross, 1979).

When infective-stage larvae are ingested by humans after eating infected mollusks or a paratenic host, the parasites are digested from the vector tissue and enter the intestinal tissue causing enteritis. Passage of the worm through the liver may also cause hepatomegaly. Cases may be benign and self-limiting, but when many worms are involved, severe central nervous system (CNS) symptoms can develop. The symptoms may be abrupt and persistent (Yii, 1976) and may be attributed partly to the destruction and inflammation of nerve fibers. Severe headache, stiff neck, nausea, vomiting, and fever as well as myalgia, pain, and paresthesia in the skin of the trunk and the limbs may develop (Punyagupta et al., 1975; Cross, 1978). There are numerous reports of ocular symptoms especially from Indonesia (Widagdo et al., 1997), Sri Lanka (Dissanaike et al., 2001), Vietnam (Thu et al., 2002), Okinawa (Toma et al., 2002), Thailand (Eamsobhana, 2005), India (Malhotra et al., 2006) and Taiwan (Liu et al., 2006; Wang et al., 2006). It is possible that the first report of human angiostrongyliasis was from Sri Lanka in 1925, when a larval worm was recovered from the eye of a patient with iritis (Dissanaike and Cross, 2004). There also was a report of sensorinneural hearing loss in a Thai patient with eosinophilic meningitis (Chotmongkol et al., 2004a).

Generalized weakness and flaccid paralysis of the extremities have been reported and, at times, coma. When the developing worms migrate from the neural tissue to the surface of the brain and cord and enter the subarachnoid space, they may cause inflammation of the meninges and the production of eosinophils. Many worms may die in the CNS and provoke more reactions and disease. The incubation of the disease is highly variable, 1 day to several weeks, depending on the number of parasites involved. Table 8.2 lists the major symptoms and signs in 114 cases of eosinophilic meningitis in Taiwan (Yii, 1976). The severity of the disease is related to the number of parasites involved and at an autopsy carried out on Taiwan, a large numbers of worms were recovered (Yii et al., 1968).

## Pathogenesis

Rats usually suffer little from infection with *A. cantonensis* except when large numbers of worms are involved. There may be cellular infiltration and edema when the parasite enters the gastric mucosa and small necrotic foci in the liver and lungs with eosinophilic and seropurulent pleurisy. Small foci of edema and hemorrhage may develop in the CNS along with granulomatous reactions.

TABLE 8.2. Major symptoms and clinical signs in cases of eosinophilic meningitis on Taiwan.

| Symptoms | Signs |
|---|---|
| Headache | Abnormal patellar reflex |
| Nausea, vomiting | Neck stiffness |
| Somnolence, lethargy | Abnormal Achilles reflex |
| Fever | Absence abdominal wall reflex |
| Constipation | Hepatomegaly |
| Malaise | Kernig's sign |
| Anorexia | Abnormal biceps reflex |
| Abdominal pain | Eye muscle paralysis |

The molted sheaths of the worm can cause granulomas with giant cells and monocytes with abscesses developing especially in heavy infections. As the infection progresses, the subarachnoid spaces become dilated with hemorrhage resulting from dilated cerebral veins. Hemorrhage also occurs in the nerve roots of the cranial and spinal nerves. Parasites in the lung arteries may cause embolism and hypertrophy with cellular infiltration in the arteries and bronchi with thrombosis in the arteries. Thrombi may encase parasite eggs and larvae along with nodular formation in the lungs parenchyma (Alicata and Jindrak, 1970).

In humans, a gastroenteritis and hepatomegaly may be experienced after eating infected intermediate hosts. Cough, rhinorrhea, sore throat, malaise, and fever may develop when the worms pass through the lungs, and when they reach the CNS, symptoms of eosinophilic meningitis and eosinophilic pleocytosis develop. There are a few reports, however, where the patients exhibited peripheral eosinophilia yet did not develop eosinophilic pleocytosis (Tsai et al., 2001; Lindo *et al.*, 2004).

It appears that dead parasites cause more pathology than living worms, and in the few autopsies carried out, both living and dead worms have been found. Living fourth- and fifth-stage worms have been recovered from subarachnoid spaces and on the surface of the brain and the cord. Upon gross examination, few lesions can be seen; however, there may be congestion and hemorrhage with thickening of the basal portion of the leptomeninges (Fig. 8.12). Histologically,

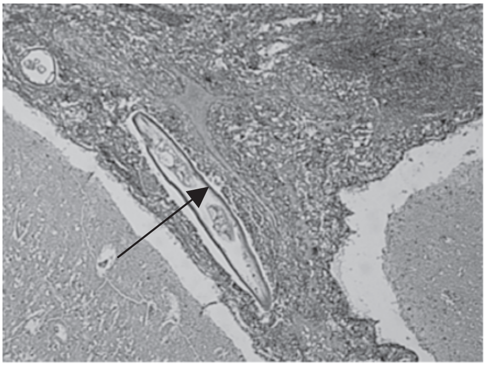

FIGURE 8.12. Section of brain showing *Angiostrongylus cantonensis* (arrow) in the leptomeninges.

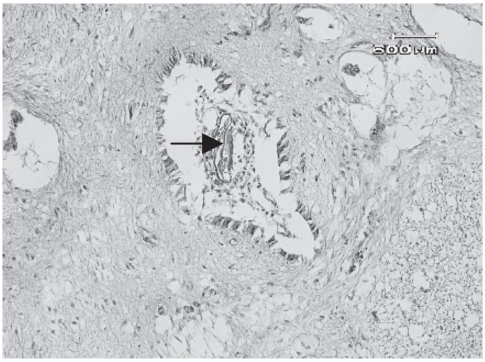

FIGURE 8.13. Section of spinal cord showing *Angiostrongylus cantonensis* (arrow) in the central canal.

the worms are not concentrated and tissue sections from different parts of the brain and the cord have to be examined in order to find them. Dead worms, the sheath, and worm fragments provoke the inflammatory reaction, eosinophils, and granulomatous reaction, including giant cells and focal necrosis (Fig. 8.13). Tracks made by the migrating worms may be seen in the tissue with the presence of glial scars containing hemosiderin, hemorrhage, eosinophils, and Charcot-Leyden crystals. There may be arterial and venous dilation in the subarachnoid spaces. Nerve cells adjacent to worms and tracks may show critical chromatolysis and axonal swelling. Similar changes occur in the spiral cord (Punyagupta, 1979).

An autopsy was carried out on a 5-year-old child in Taiwan who died with eosinophilic meningitis. Tissues were examined and sections of the parasite were detected in the brain (Fig. 8.14), spinal cord (Fig. 8.15) and lungs (Fig. 8.16).

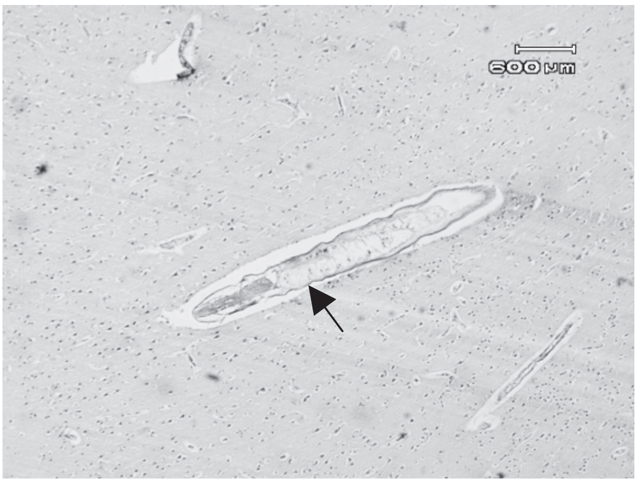


FIGURE 8.14. Section (arrow) of *Angiostrongylus cantonensis* in the parenchyma of the brain showing little inflammatory reaction.

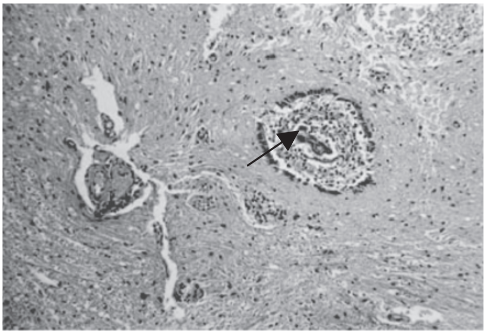

FIGURE 8.15. Section of *Angiostrongylus cantonensis* in the central canal of the spinal cord (arrow) surrounded by an intense inflammatory reaction.

The leptomeninges were infiltrated with lymphocytes, pigment-laden macrophages, and mononuclear cells (Fig. 8.17). Foreign-body–type giant cells were found close to degenerative worms (Fig. 8.18). Cerebral and cerebellar sulci sections revealed sections of viable worms (Fig. 8.19). Lymphocytes surrounded cerebral and meningeal vessels. Numerous glial elements and glitter cells were also in these regions. There was also perivascular cuffing by lymphocytes. Foreign-body reaction surrounded dead worms and recently dead parasites provoked a mixed reaction of mononuclear cells, lymphocytes, and eosinophils. Over 500 immature and young adult worms were recovered from the CNS, and developing eggs were found in the uterus of some female worms. The lungs were congested, and macrophages with pigments were found in the alveolus. Proteinaceous material and neutrophils infiltrated around the bronchi and bronchioles. Focal hemorrhages were seen and some small blood vessels contained thrombi. Living worms were found in pulmonary vessels (Figs. 8.20 and 8.21) (Yii et al., 1968). Worms in the lungs have also been reported from another Taiwan patient (Hung and Chen, 1988) as well as patients in Australia (Cooke-Yarborough et al., 1999), Jamaica (Lindo et al., 2004), and in Thailand (Eamsobhana, 2005).

The parasite has also been found to infect primates with the pathological findings similar to those reported from humans. Monkeys given as many as 10,000 larvae

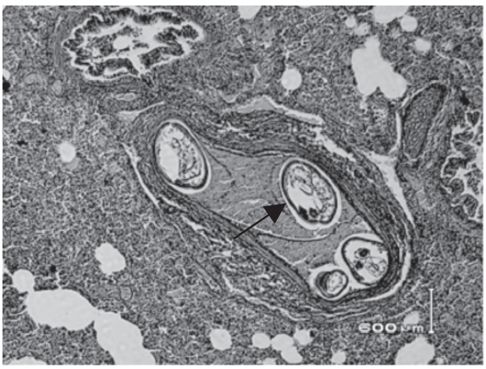

FIGURE 8.16. Section of *Angiostrongylus cantonensis* (arrow) in a pulmonary artery of a human.

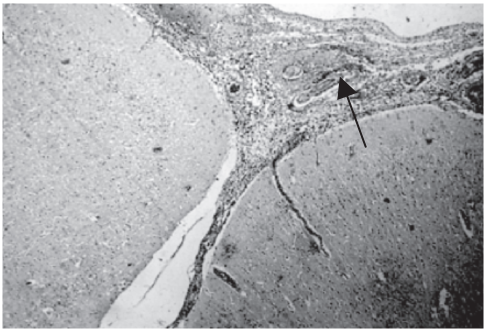

FIGURE 8.17. Section of *Angiostrongylus cantonensis* (arrow) in the leptomeninges surrounded by inflammatory cells.

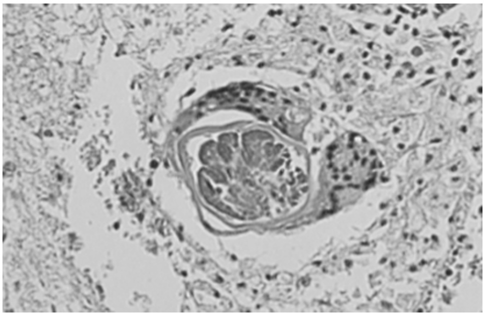

FIGURE 8.18. Section of the spinal cord showing a degenerated *Angiostrongylus cantonensis* surrounded by a foreign-body giant cell.

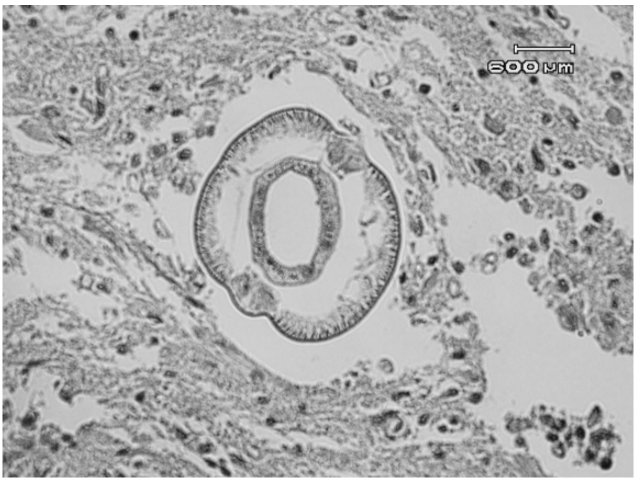


FIGURE 8.19. Section of human brain showing *Angiostrongylus cantonensis* without inflammatory reaction.

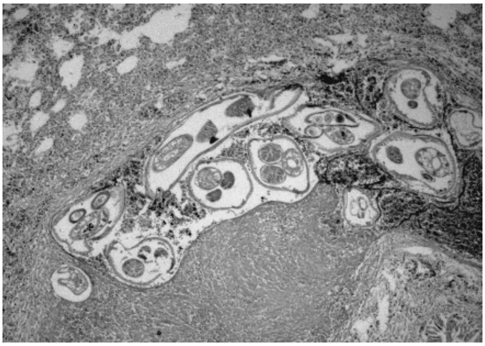

FIGURE 8.20. Human lung showing multiple section of *Angiostrongylus cantonensis* in a pulmonary artery.

usually died, and at necropsy little tissue reaction was seen around the worms in the CNS of animals examined early (10 days) in the infection (Fig. 8.22). However, cellular infiltration around worms consisting of eosinophils, plasma cells, lymphocytes, giant cells, and perivascular hemorrhage were found at 29 days postinfection (Fig. 8.23). The reactions were associated with dead worms rather than living worms. In early infections, the worms were still in the third stage, while those found later were in the fourth larval stage or young adults (Cross, 1979).

## Diagnosis

A confirmed diagnosis for *A. cantonensis* eosinophilic meningitis is rare. In areas endemic for the parasitosis, diagnosis is usually presumptive based on the symptoms of headache, nausea, vomiting, fever, neck stiffness, paresthesia, diplopia, and strabismus, and a history of contact or ingestion of an intermediate or paratenic host. Cerebro spinal fluid (CSF) may demonstrate eosinophilic pleocytosis, hemorrhage, and occasional xanthochromia. The confirmed diagnosis is based on the recovery of larval stages of the parasite in CSF (Fig. 8.24) (Kuberski *et al.*, 1979) or from ocular chambers (Fig. 8.25). Recovery of worms from the

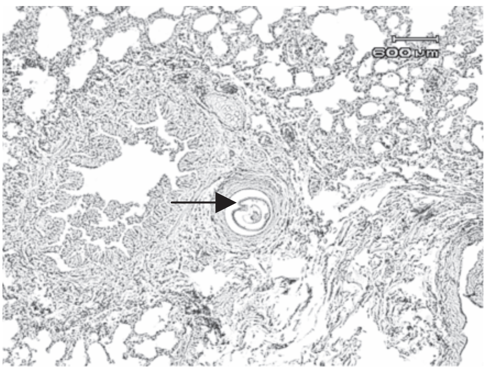


FIGURE 8.21. Human lung with section of *Angiostrongylus cantonensis* (arrow) in a pulmonary vessel.

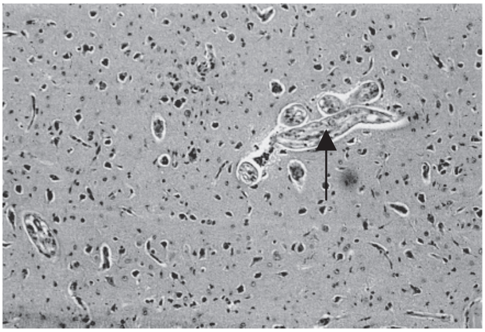

FIGURE 8.22. Section of *Angiostrongylus cantonensis* in the brain parenchyma of a monkey 10 days post-infection showing little reactions.

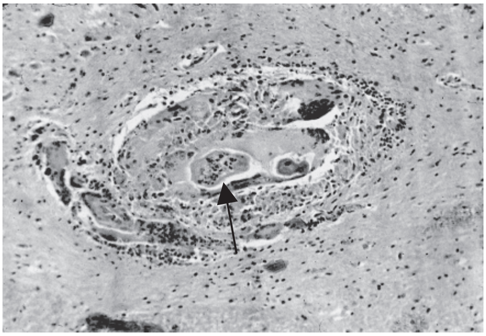

FIGURE 8.23. Section of a monkey brain 29 days after infection with *Angiostrongylus cantonensis* showing an intense foreign-body giant cell reaction around degenerating worms.

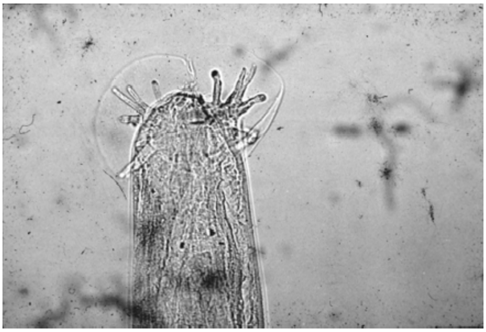

FIGURE 8.24. Young adult male *Angiostrongylus cantonensis* recovered from the spinal fluid of a Taiwanese child. (Courtesy of Dr. K.P. Hwang.)

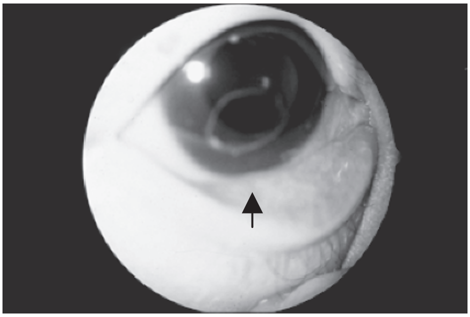

FIGURE 8.25. Larva of *Angiostrongylus cantonensis* (arrow) in the eye of a Taiwanese child. (Courtesy of Dr. K.P. Hwang.)

CSF has improved (Hwang and Chen, 1991). Serological tests such as the enzyme-linked immunosorbent assay (ELISA) has been found to be satisfactory (Cross, 1978; Cross and Chi, 1982; Jaroonesama et al., 1985), and a number of improved immunological tests have been developed for both antibody and antigen detection (Chye et al., 2004; Maleewong et al., 2001; Eamsobhana and Tungtrongchitr, 2005). A dot-blot ELISA using blood dried on filter paper has proven to be convenient for handling field samples for epidemiological surveys (Eamsobhana and Tungtrongchitr, 2005; Eamsobhawa et al., 2006). Antigens from *A. cantonensis* can also be detected in serum by immuno–polymerase chain reaction (PCR) (Chye et al., 2004). Computed tomography (CT) and magnetic resonance imaging (MRI) may reveal the presence of lesion in the meninges (Jin et al., 2005).

Eosinophilic meningitis may be caused by other infectious agents as well as malignancies. Paragonimiasis, schistosomiasis, neurocysticercosis, and gnasthostomiasis should be considered in the differential diagnosis of eosinophilic meningitis.

## Treatment

Most cases of angiostrongyliasis are mild and self-limiting, with symptoms abating in 4 to 6 weeks. Treatment is supportive or symptomatic using analgesics with corticosteroids (Pien and Pien, 1999) and frequent removal of CSF to relieve increasing intracranial pressure and to relieve headaches. Specific anthelminthic treatment is controversial since dead worms are considered by some to cause more pathological changes. However, mebendazole and albendazole have been reported effective in treating children (Hwang and Chen, 1991), and a combination of albendazole and corticosteroids has also been reported as effective treatment (Chotmongkol et al., 2006). A recent study has suggested that a Chinese herbal medicine, yin-chen extract, in combination with albendazole may be effective in managing eosinophilic meningitis or eosinophilic meningoencephalitis (Lai, 2006). Worms in the eye usually require surgical removal (Kumar et al., 2005); however, paralysis of the parasite with intracameral preservative-free lidocaine provides easy removal of the worm (Mehta et al., 2006).

## Epidemiology

*Angiostrongylus cantonensis* is found in most tropical areas with warm moist environments where rodent definitive hosts and molluscan intermediate hosts abound. *Rattus rattus* and *R. norvegicus* are the most common definitive host, but other species of rats found in rural and forested areas such as *R. exulans, R. diardii, R. coxinga, R. argentiventer, R. losea, R. jalorensis, R. tiomanicus, R. mindanensis*, and *Bandicota indica, B. savilei*, and *B. malobarica* are also reported to be natural hosts. It is quite possible that all species of *Rattus* or *Bandicota* are susceptible to infection. Although other species of mammals can be infected, the parasite is usually unable to complete its development and the "abnormal" host commonly dies when a large number of worms are involved. The worm has been reported to cause death to primates in zoos in the United States (Gardiner et al., 1990; Aguilar et al., 1999) and Australia (Carlisle et al., 1998).

Rats, humans, and other accidental animal hosts acquire *A. cantonensis* infection by eating molluscan intermediate hosts harboring third-stage larvae of the parasite. Terrestial and some aquatic snails and slugs are the primary sources of infection. The infective larvae are encysted in the tissues of the hosts (Fig. 8.8) and the larvae released upon ingestion and digestion of the tissue. Most species of mollusks are susceptible and are capable of transmitting the worm; however, the intensity of the infection is variable. The giant African snail, *Achatina fulica,* is considered a major source of infection, and, according to Alicata and Jindrak (1970), the dispersion of the parasite is associated with the spread of the snail throughout Asia and the Pacific Basin. Once established in a country, local mollusks acquire the parasite and rats become infected by eating the infected mollusks. *Angiostrongylus cantonensis*–infected mollusks were probably introduced worldwide, initially by ship traffic or by migrating human populations that include the snail as part of their diet (Kliks and Palumbo, 1992; Cross, 2004). It is also believed that heavy ship traffic during World War II may have been a means of dispersal of snails throughout Asia and the Pacific Islands. The hitch-hiking snails could have been hiding in heavy equipment moving around the war zones.

*Achatina fulica* is a large terrestrial snail (Fig. 8.26) with an enormous reproduction potential, and when introduced to an area, becomes a serious problem to agriculture. The snail may be eaten cooked, and, when mixed with various seasoning, eaten uncooked. It is also possible for larvae to be released during preparation of the snail when released larvae contaminate the knives or chopping blocks that are subsequently used for cutting other foods. Some populations also use snails and juice from snails for medicinal purposes.

Other species of snails throughout the world that are known vectors of *A. cantonensis* include *Cryptozona bristalis, Bradybaenae similaris, Macrochlamys resplendens, Subulina octona, Pila ampullacea, P. polita, P. scutata* (Fig. 8.27), *Ampullarium caniculatus, Ampularia gigas* and the rice-paddy snail, *Cipangopaludina chinensis*

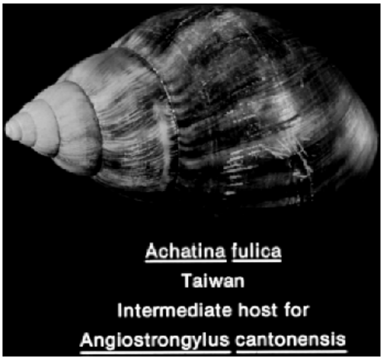


FIGURE 8.26. *Achatina fulica* an important intermediate host and vector for *Angiostrongylus cantonensis* in the Asia Pacific area.

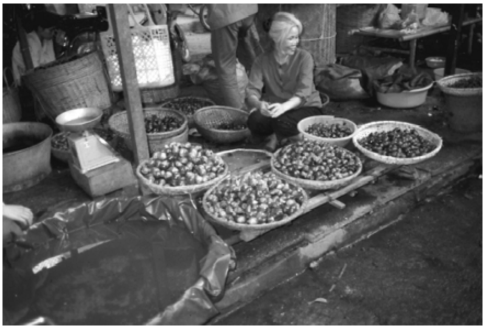

FIGURE 8.27. Baskets of *Pila* sp. snails. An important intermediate host of *Angiostrongylus cantonensis* being sold in a market in Thailand.

(Fig. 8.28). Many species of snails have been experimentally infected reflecting the widespread susceptibility of snails to infection (Richards and Merritt, 1967; Wallace and Rosen, 1969). Slugs in various endemic areas are also known vectors. *Vaginalus plebeius* (Fig. 8.29), *Veronicella alte, Decerocerus laeve, Parmarion martens, and Microparmarion malayanus* have been found to be infected or susceptible to infection and able to serve as intermediate hosts.

A large number of animals are known paratenic hosts. Land crabs, coconut crabs, and freshwater prawns are known paratenic hosts and are eaten raw (Alicata, 1962). Frogs have been considered a paratenic host (Ash, 1968), and one human case of eosinophilic meningitis has recently been reported in a man who ate, on a dare, two uncooked green tree frog legs in Louisiana in the United States

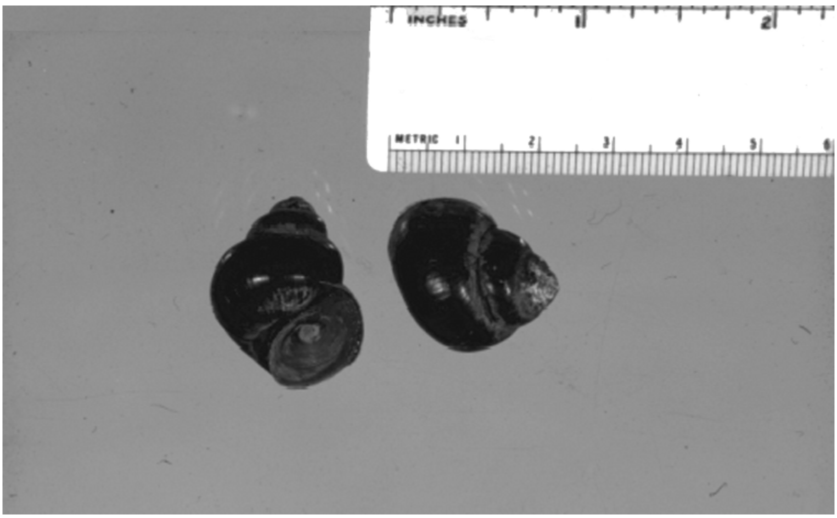


FIGURE 8.28. Rice paddy snail (*Cipangopaludina chinensis*) responsible for an infection of *Angiostrongylus cantonensis* in a Taiwan child. The child ate the snails directly from a rice paddy.

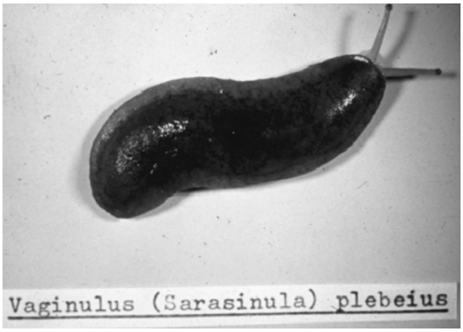


FIGURE 8.29. The slug *Vaginalus plebeius*, an intermediate host and vector for *Angiostrongylus cantonensis.*

(Cuneo et al., 2006). Eating raw liver of a toad has also been implicated in infections in Japan (Kinjo et al., 1975). Juice from crushed crustaceans is also a source of infection. Planarians are also considered a source of infection in some areas. These flatworms are predaceous on dead or dying snails and slugs and subsequently acquire third-stage larvae. Humans become infected when eating the planaria on uncooked vegetables. In New Caledonia, there is an increase of human infections in the cool season, a time when there is an influx in planaria in vegetable gardens (Ash, 1976). The tiny organisms are unseen and accidentally ingested when eating uncooked vegetables. Human infections have also been reported in people that ate raw or partially cooked monitor lizards in Thailand (Eamsobhana and Tungtrongchit, 2005), Sri Lanka (Hidelaratchi et al., 2005), and India (Panackel et al., 2006).

In Taiwan, most eosinophilic meningitis is seen in children and most have been associated with eating *A. fulica* meat. The snail is usually heavily infected and consequently causes more disease. In Thailand, on the other hand, most infections occurred in adult males who ate Pila spp snails (Fig. 8.27), a poor host that contain few infective stage larvae (Eamsobhana and Tungtrongchitr, 2005). The symptoms therefore are milder. Thai men acquire the infections primarily at the time of drinking alcohol with friends. Thai men also feel that the snails have some medicinal value. *Achatina fulica* has become a commercial value in Taiwan and other places and are raised commercially for the meat used in the preparation of escargot (Fig. 8.30). In a preliminary study on Taiwan, snail meat in a market in southern Taiwan was fed to laboratory rats. Some of the meat had been cooked and some uncooked. Every rat fed with the uncooked meat developed infections with *A. cantonensis,* while the animals fed cooked meat were negative at necropsy.

In 1976, three U.S. Marines on survival training in Okinawa, Japan, ate five to 10 *A. fulica* uncooked. Several other Marines tasted the snails while others ate only cooked snails. Three weeks after eating the raw snails, the three Marines became ill and were hospitalized. They had symptoms of eosinophilic meningitis and were serologically positive. The hospital course was uneventful, although one required ventricular drainage and repeated lumbar punctures. The Marines who ate the

FIGURE 8.30. Empty shells of *Achatina fulica* that have been raised and provided the meat for export for the preparation of escargot.

cooked snails and those who only tasted the snails had no ill effects (Cross, 1978). Group infections have been reported such as the event in Samoa when six Koreans were sold, as a prank, living *A. fulica* by the native Samoans. The Koreans ate the snails raw and became severely ill and one died (Kliks et al., 1982). The first case of eosinophilic meningitis in the United States occurred when a child in New Orleans, Louisiana, was dared by his sister to eat a live snail (New et al., 1995).

Water may also be a source for infection. Terrestrial mollusks falling into water may drown and release larvae into the water (Alicata and Jindrak, 1970; Crook et al., 1971). There is also a report from Taiwan reporting an outbreak of eosinophilic meningitis by drinking vegetable juice probably contaminated with a small intermediate or paratenic host or infective larvae in molluscan mucus deposited on the vegetables (Tsai et al., 2004). Another interesting report from Taiwan was a boy who acquired the disease while raising *A. canaliculatus* as pets (Wan and Weng, 2004), and in mainland China 18 people who ate these snails raw also developed the disease (Wang et al., 1999). There are an increasing number of cases of angiostrongyliasis reported from China (Chen et al., 2005), and many of the patients had eaten snails from one particular restaurant in Beijing specializing in the dish. The snails involved were called Amazon snails (*Ampularia gigas*) that originated from South America and introduced into China in 1980. A total of 137 cases were reported by the Xinhua News Agency in September 2006.

## Impact and Issues

There are relatively few problems associated with angiostrongyliasis. Human infections are sporadic and are rarely seen even in endemic areas.

In April 2003, 12 of 23 tourists who visited Jamaica met the case definition of eosinophilic meningitis. No parasites were found in the CSF, but 11 of the 12 had positive antibody titers. The source of infection was not determined, but the tourists all had eaten a salad in a restaurant (Slom et al., 2002). Events such as this can make an impact on the tourist industry. Cases of eosinophilic meningitis have been reported in the Jamaican population, with at least one death and the parasite has been isolated in rats and snails (Lindo et al., 2002).

*Angiostrongylus cantonensis* has also had an impact on zoos. The death of primates in the Audubon Park and Zoological Garden in New Orleans, Louisiana, was of great concern to the veterinarians (Gardiner et al., 1990; Aguilar et al., 1999). Death was also reported in a gibbon from the Miami, Florida, Metrozoo. The monkey had been in the zoo since 1963, and the parasite was recovered from the CNS (Duffy et al., 2004). A lemur in a zoo in New Iberia, Lousiana, was also found to be infected (Kim et al., 2002). If there is an increase of the parasite in the rat population, other wildlife species such as the wood rat and opossums may acquire fatal infections (Kim et al, 2002). The parasite has also been found in a miniature horse in Louisiana (Costa et al., 2000). It is anticipated that *A. cantonensis* will continue to remain endemic in the southern United States, and the spread of the parasitosis in nature will undoubtedly lead to human infection and disease.

Only one other species of *Angiostrongylus* is known to cause disease in humans. *A. costaricensis* is in Latin America and is known to cause eosinophilic granuloma in the human intestines (Morera and Cespedes, 1971; Cross, 1998). The definitive hosts of the parasite are cotton rats (*Sigmodon hispidus*) and black rats (*Rattus* sp.). Infections have also been reported in animals in the Miami, Florida, Metrozoo (Miller et al., 2006). Slugs (*Vaginulus plebeius*) serve as the intermediate host. Humans acquire the infection accidentally by ingesting infected slugs or vegetations that have slug mucus trails containing infectious-stage larvae. The larvae from the slugs penetrate the intestinal wall of the rat and mature in lymph nodes and lymphatic vessels. The young worms migrate to the mesenteric arteries and lay eggs. The female worms lay eggs in the intestinal wall. They hatch and the larvae migrate into the intestinal lumen. In humans, eggs and any hatched larvae are usually destroyed by the cellular reaction and the parasite products are not found in the feces. The inflammatory reaction results into the formation of a mass and in some cases may partially or completely obstruct the intestines. Most lesions are found in the appendix. Surgical removal is the treatment, and anthelminthics are not recommended. Most cases involved children, and while the parasitosis is reported throughout Latin America, Costa Rica reports a significant number of cases each year (Sun, 1998). A parasitologic diagnosis is not available and the serological diagnosis presents several drawbacks. However, PCR technologically is reported to be an alternative (da Silva et al., 2003; Caldeira et al., 2003).

## Unsolved Problems

There is a need to determine the geographic distribution of *A. cantonensis* in wildlife populations of rats and mollusks. This requires surveys (especially for rat infections), support funds, and man hours. Rats would have to be trapped and killed and the heart and lungs examined for worms. Once found in rats, surveys should be carried out to determine infection in snails and paratenic hosts.

Public health workers and physician in endemic areas must be made aware of the parasite, its hosts, and the dangers to the health of populations. Programs should be developed to make the indigenous populations aware of the problems and to warn them about eating mollusks and paratenic hosts uncooked. More specific and sensitive diagnostic techniques must be developed. It is difficult to make a parasitological diagnosis, as worms are not easily detected antemortem. Serological and molecular tools are available, but are only used at a few universities and research centers in Asia, and the tests are not always conclusive.

It would be interesting to determine if strains of the parasite exist. In a study of strains of *A. cantonensis* from Asia and Hawaii, a new species, *A. malaysiensis,* was discovered (Cross, 1979). There are now four different species of *Angiostrongylus* found in Southeast Asia and Australia: *A. cantonensis* (Chen, 1935), *A. mackerrasae* (Bhaibulaya, 1968), *A. malaysiensis* (Bhabulaya and Cross, 1972; Cross and Bhaibulaya, 1974), and *A. siamensis* (Ohbayashi et al., 1979). The four species are found essentially in the same intermediate and definitive host; however, only *A. cantonensis* has been confirmed to be the cause of human eosinophilic meningitis. It is possible, however, that *A. mackerrasae* in Australia (Prociv and Carlisle, 2001) and *A. malaysiensis* in Malaysia (Ambu et al., 1997) may infect humans.

## Control

The control of *Angiostrongylus* species in nature is very difficult. However, rodent control in areas close to human communities is recommended. The elimination of molluscan hosts of the parasite near housing and vegetable gardens should be routine. Populations in endemic areas should be made aware of the parasite, the host the means of transmission, and the possibility of illness. The habit of eating uncooked snails and paratenic hosts should be discouraged. Vegetation should be examined for snails, slugs, or planaria and washed thoroughly if eaten raw; however, cooking vegetables is recommended. Natural water should not be drunk unless boiled. It is difficult to change eating habits of the population that have existed for generations, but it would be necessary to prevent infection with *A. cantonensis*.

The spread of *A. cantonensis* has been attributed to the introduction of *A. fulica* accidentally to Asia and the Pacific Basin. This may have contributed to the dispersal of the snail initially, but in most recent times it is believed the spread has been considered to be via ocean shipping. Snails are known to be in ship cargo and can be carried ashore. However, the transporting of rats via ship is probably the most accepted means of dispersal of the parasite. Therefore, snail and rodent control measures should be employed on ships.

## Summary

*Angiostrongylus cantonensis* is a metastrongyle nematode considered an important cause of eosinophilic meningitis in areas endemic for the parasite. Adult worms are found in the pulmonary vessels of *Rattus* and *Bandicotta* species, and larvae from eggs deposited in the lung migrate to the intestine and pass in the feces. The larvae are ingested by snail and slug intermediate hosts and develop into the infective stage of the worm. When intermediate hosts are eaten by a definitive host, the larvae migrate to the brain. Young adult worms that develop after a few weeks migrate from the brain to the pulmonary vessels, where they complete development and reproduce.

Humans become infected by eating an intermediate or paratenic host (planaria, amphibians, crustaceans, lizards) raw or poorly cooked. The larvae are digested from the animal tissue, and like the rodents, the larvae migrate to the brain and cause disease. The important signs and symptoms are headache, stiff neck, nausea, vomiting, myalgia, paresthesia, and eosinophilia pleocytosis, and on rare occasions the parasite may complete development in humans with worms found in the lungs at autopsy. There are reports of *A. cantonensis* invading the eye. The disease may persist for several weeks and is usually limiting.

The parasite was first reported in rats in China but was thought to have originated in Africa and spread eastward, possibly carried by the giant African snail, *Achatina fulica*. Human infection was first reported from Taiwan in 1945. It was not until 1961, however, when the parasite was found in the brain of a man at autopsy in Hawaii. It was not too long before the parasite and disease was reported throughout the Far East and the Pacific Basin. The disease is now recognized in many parts of the world and has reached the Western Hemisphere. Most reports of the parasite and disease are from Taiwan and Thailand with increasing reports from the China mainland. The parasite has reached the United States, with reports of infection in rats, molluscan intermediate hosts, some abnormal host animals, and two human cases of eosinophilic meningitis.

The cause of clinical disease is questionable. Some physicians believe that reaction to dead worms are responsible for the pathology and do not recommend anthelminthic treatment. There are a few physicians, however, who report successful treatment with mebendazole, or albendazole along with a steroid. Worms found in the eye are removed surgically.

The parasite is on the move. The dispersal is possibly due to rats and snails that are stowaways in cargo aboard sea-going ships. When the ships reach port, the rats jump ship and the snails in cargo are moved ashore. Control of the parasite in nature is nearly impossible, but community control measures could be implemented. Changes in eating habits can be difficult, but populations in endemic area should be made aware of the dangers of eating snails and paratenic hosts raw. The populations should also be informed of hazards of accidentally eating slugs and planaria that are often found in gardens and on vegetables.

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