ANGIOSTRONGYLUS (*PARASTRONGYLUS*) *CANTONENSIS* IN THE WESTERN HEMISPHERE

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Abstract. *Angiostrongylus (Parastrongylus) cantonensis*, the rat lungworm, was once considered primarily endemic to Asia and the Pacific Basin. The nematode was first described from China, but throughout the years has been reported worldwide in rats, the molluscan intermediate host as well as humans. *Angiostrongylus* eosinophilic meningitis was first reported from Taiwan, followed 17 years later from Hawaii where a man died and the worm found in his brain. The parasite was not known to be in the Western Hemisphere until reports of eosinophilic meningitis in Cuba. Subsequently, the intermediate molluscan and definitive rodent hosts, as well as human infections, have been reported from many of the Caribbean Islands. In the continental United States, *A. cantonensis* was found in rats in New Orleans, Louisiana and locally collected molluscs were susceptible to experimental infections. The parasite was next found in primates in the Audubon Zoo in New Orleans. Snails and slugs collected from the zoo environment were also found infected with the larval stages of the parasite. One human case from Louisiana has been documented and more recently 12 American travelers to Jamaica returned home with the disease. The parasite is on the move with reports of infections in a horse from Mississippi and wildlife in Louisiana. There is now concern that in time the parasite will spread to infect wild and domestic animals and possibly humans elsewhere in the country. The question remains on how the parasite has moved from East to West. It may have been via infected molluscs stowawayed on ocean going ships, or more likely by infected stowaway rats that "jumped" ship and infected local molluscs. Many species of mollusc are susceptible to infection and are able to serve as intermediate host, but only rats can serve as definitive hosts.

INTRODUCTION

Angiostrongylus cantonensis is a classic example of an "emerging" parasitic disease. Since it was first described, the parasite and its intermediate and definitive hosts have been reported from various parts of the world and are definitely on the move.

Twenty species of *Angiostrongylus* have been found in a variety of animals, however only 2 species have been reported affecting humans; *A. costarecensis* found in the mesenteries of rodents in the Americas with a few human infections and *A. cantonensis*, which is found in the pulmonary blood vessels of the rat and is now reported worldwide in rodents as well as humans.

Angiostrongylus cantonensis was first described as *Pulmonema cantonensis* from the lung of rats by Chen (1935) in South China. Matsumoto (1937) and Yokogawa (1937) found the nematode in the lung of rats in Taiwan and it was named *Haemostrongylus ratti*. Dougherty (1946) synonymized *Pulmonema* with *Angiostrongylus* calling it *A. cantonensis*. Ubelaker (1986) transferred the parasite to the genus *Parastrongylus* but this has not yet been universally accepted.

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HOST

Rats infected with the lungworm have been reported widely (Alicata and Jindrak, 1970; Kliks and Palumbo, 1992). *Rattus rattus, R. norvegicus*, *R. exulans, R. diardii, R. coxinga, R. agentiventer*, as well as *Bandicota indicata* and *B. malobarica* are known definitive hosts. Infections are reported from other species but the parasite has been unable to complete development in these animals.

There are many molluscan intermediate host; the land snails *Achatina fulica* and *Bradybaena similaris, Hemiplecta sagittfera, Helicostyle macrostoma*, aquatic snails *Pila ampullacea, P. scutata, Cipangopaludina chinensis, Ampullarum* spp and slugs *Vaginulus plebeus, Veronicella alte* and *Derocerus laeve*. Many species of molluscs can serve as experimental intermediate host and known paratenic hosts are freshwater prawns and crabs, land crabs, frogs, toads, and planarians. Vegetables eaten unwashed and uncooked may harbor small infected intermediate or paratenic host and larvae may be in mucus deposited by slugs onto vegetables. The giant African snail, *A. fulica* eaten uncooked by children, is an important host in Taiwan and other Asian Pacific

areas. In Thailand, however, *P. ampullacea* is a major source of infection and in the Pacific Islands, prawn and juice from prawn are sources of infection. These animals are also used for medicinal purposes and as such have been incriminated in human infections.

Most human diseases have been reported from Taiwan, where the first human case was reported (Nomura and Lin, 1945), Thailand, and a number of the islands in the Pacific basin with sporadic reports from other areas of Asia, Africa, Australia, South Asia, and islands in the Indian Ocean.

LIFE CYCLE

Rats

Adult *A. cantonensis* is in the pulmonary arteries of rats. Female worms produce eggs that lodge in the capillaries of the lung. First-stage larvae develop and emerge from the egg, break through the capillaries into the alveoli and migrate into the bronchioles. The young worms pass up the pulmonary tree are swallowed and pass out in the rat feces. The larvae are ingested or penetrate a molluscan host and migrate to muscle. The larvae develop into the second- and third-stages in about 2 weeks. When the molluscs are eaten by rats, the larvae are digested out of the muscle, penetrate the intestinal mucosa, enter the circulatory system and carried to the central nervous system (CNS) within 24 hours. The worms develop into young adults, migrate to the pulmonary arteries, mature into adults and reproduce in about 6 weeks.

Humans

In humans, after ingestion of an infected mollusc or paratenic host, the third-stage larvae migrate to the CNS like in the rats. The parasite will develop into young adults and usually do not develop further. Only on a few occasion has the parasite reached the lung of humans and reproduced (Cross, 1987). Major symptoms of infection in humans are headache, nausea and vomiting, fever, stiff neck, paresthesias, paralysis of the eye muscle, and somnolence. The cerebral spinal fluid (CSF) contains leukocytes, mostly eosinophils and occasionally young adult worms. Worms have also been recovered from the eye. The incubation period is variable, 1 to 30 days. The diagnosis of human infection is based on symptom and a history of exposure to intermediate or paratenic hosts. The definitive diagnosis is the presence of young adult worms in the spinal fluid. ELISA testing and antigen detection test of sera and CSF are proving valuable (Cross and Chi, 1982; Eamsobhana and Dechkum, 2000).

Specific treatment is debatable. Some physicians recommend no treatment as massive killing of the worm may cause more pathology. However, children in Taiwan have been successfully treated with mebendazole and albendazole (Hwang and Chen, 1991).

WESTERN HEMISPHERE

Angiostrongyliasis cantonesis has been reported from several Caribbean Islands as well as the United States (Fig 1). The first report of the parasitoses in humans was reported from Cuba by Pascual *et al* (1981), and in rats and pooled lots of molluscs by Aguiar *et al* (1981). Human infections continue to be seen in Cuba (Dorta-Contreras and Reiber, 1998; Martinez-Delgado *et al*, 2000) with one report of lung infection (Cadilla *et al*, 1998). The mode of transmission has not been determined and Cubans usually do not eat uncooked molluscs or crustaceans and raw vegetables are rarely eaten. Infections are probably from the accidental ingestion of intermediate hosts (Pascual *et al*, 1981). Perera *et al* (1983) have reported finding 11 species of Cuban molluscs naturally infected with the parasite.

Rattus rattus and *R. norvegicus* were found in Puerto Rico infected with adult worms and the snails, *Subulina octona* and *Aquebana belutina*, were found infected with larval stages (Anderson *et al*, 1986). One suspected human infection has been reported based upon a positive ELISA test (Cross, 1987).

Rattus rattus and the snail *Sublina octona* were reported with *A. cantonensis*, in the Dominican Republic (Vargus *et al*, 1992).

In Jamaica, a human infection was reported by Barrow *et al* (1996), rats and snails were examined after a number of cases of eosinophilic meningitis were reported from tourist who visited the island. *R. rattus*, *R. norvegicus* were found infected with adult worms and the snail *Thelidomus asper* was positive for *A. cantonensis* larvae (Lindo and Waugh, 2002). *Rattus rattus* and *R. norvegicus* have recently been found infected in Haiti (Raccurt, 2003). The land snail *Achatina fulica* an important intermediate host for the parasite in Asia has now been reported in Brazil. The snail was introduced and bred for human consumption as "escargo" (Teles *et al*, 1997; Vasconcellos and Pike, 2001). However, no parasites were recorded. In an unpublished report, the sera from symptomatic children from Guadalupe tested positive for the disease, but the parasite has yet to be reported in animals.

The first report of the parasite in the continental

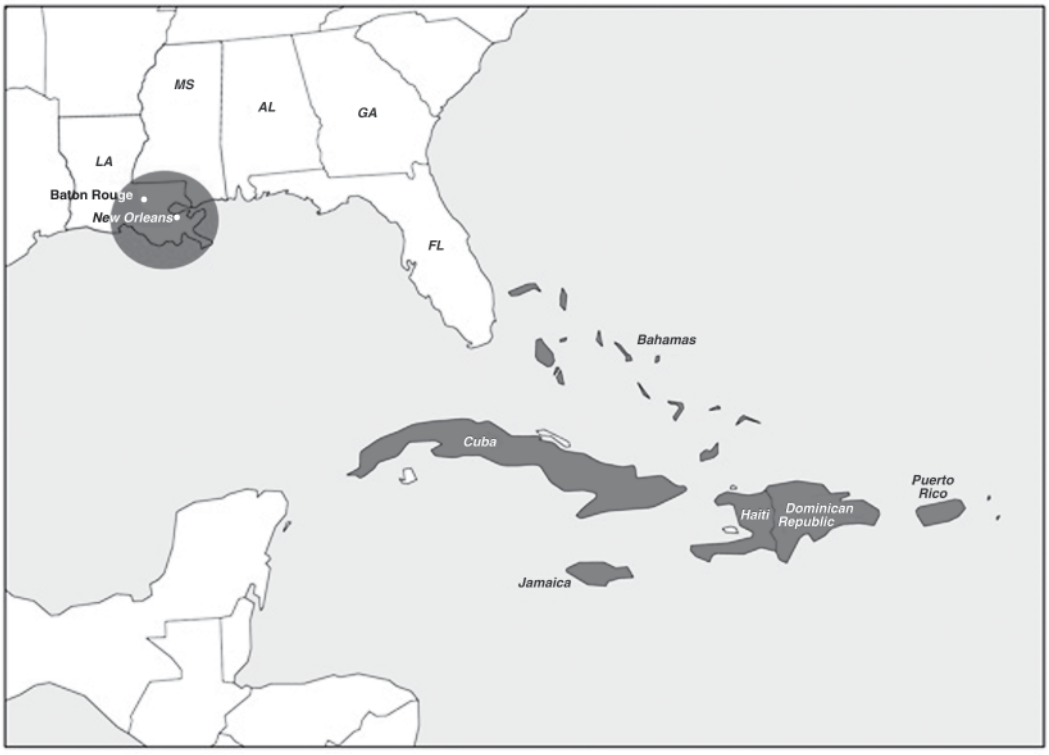

Fig 1- *Angisotrongylus cantonensis* in the Western Hemisphere.

United States was by Campbell and Little (1988). Adult worms were recovered from 20 *R. norvegicus* in New Orleans, Louisiana. Several species of gastropods, although not found naturally infected, were susceptible to experimental infections. The rats were live-trapped at various sites at wharves along the Mississippi River.

Gardiner *et al* (1990) reported fatal meningoencephalitis due to *A. cantonensis* in the howler monkey *Alaceatta carrya* at the Audubon Park and Zoological Gardens in New Orleans. The same paper reported infection in a white-handed gibbon (*Hylobates lar*) from the Ardastra Gardens and Zoo in Nassau, Bahamas. The animals had access to free-ranging gastropods in the zoos. Several years later, Aguilar *et al* (1999) reported angiostrongyliasis in 3 black and white ruffed lemurs (*Lemur variegatus*), and a talapoin monkey (*Cercopithecus talapon*), in the Audubon Zoo in New Orleans. Other animals in the zoo also exhibited symptoms of angiostrongyliasis. The absence of infections in monkeys between reports is attributed to control of snails and slugs from exhibit areas. Intermediate hosts recovered after the second report were found infected with larval stages of the parasite.

In 1995, New *et al* reported an infection in an 11-year old boy in New Orleans. This would be the first human infection in North America. The boy had eaten a raw snail on a dare. The boy had typical symptoms of eosinophilic meningitis and sera from the boy tested positive.

The parasite has now moved from the New Orleans area and has been reported in areas north of the city. Costa *et al* (2000) reported meningoencephalitis caused by *A. cantonensis* in a miniature horse from Picayune, Mississippi, approximately 87 km from New Orleans and in the same report *R. norvegicus* trapped in Baton Rouge, Louisiana, 124 km from New Orleans were positive for the parasite. In a more recent report, Kim *et al* (2002) found the infection in a lemur (*Varencia variegata ruba*) from New Iberia, Louisiana, 222 km from New Orleans and a wood rat (*Neotoma floridanus*) and 4 opposums (*Didelphis virginiana*) from Baton Rouge. The authors stated that the potential of a variety of snails and slugs in Louisiana pose a great threat to wildlife and domestic animals. Other human infections may occur but it is only on rare occasion will Americans eat uncooked intermediate or paratenic hosts. Infections, however, can be

accidental when individuals unknowingly eat an infected intermediate hosts.

An outbreak of eosinophilic meningitis caused by *A. cantonensis* occurred in American travelers to the Caribbean. A group of 23 tourists from Chicago and other cities traveled to Jamaica. Twelve of 23 developed symptoms and signs of eosinophilic meningitis including headache, neckache, backache, nausea, visual disturbances, muscular rigidity, paresthesia and hyperesthesia. Nine were hospitalized. Eight of the patients had eosinophils in the CSF. No parasites were found in the CSF but antibodies against *A. cantonensis* antigen were detected in the convalescent-phase sera of 11 patients. The source of infection is not known, however, a common meal eaten before departing for the United States was the suspect. The meal consisted of Caesar salad with lettuce the salad ingredient (Slom *et al*, 2002).

DISCUSSION

Over the years, *A. cantonensis* has spread from Asia, East to West, North to South. How this spread has been accomplished remains an enigma. It has been suggested that the spread was due to the dispersal of the major snail host in Asia, *A. fulica*. This may have been possible via the movement of supplies and equipment from endemic to non-endemic areas in which molluscs may have been trapped. It is known that military equipment returned to the United States often contained hidden gastropods. These snails may have been infected with *A. cantonensis*, and when eaten by indigenous rats, introduced the parasite. It has been suggested by Kliks and Palumbo (1992) that Cuba acquired a variety of agricultural and manufactured goods from Indochina during 1966-1975. Snails as well as rats could have stowawayed in these supplies. Indo-chinese infected rats could also be transported to Cuba in returning vessels. Stowawayed rats are considered the major means of spread, however. Kliks and Palumbo (1992) also suggested the spread of the parasite in the Caribbean may have been the trafficking of illicit narcotics throughout the area and rats could have been hiding in such cargo. If Cuba was the first port of entry, then the parasite could have spread to Puerto Rico, to other islands, and to the United States. The introduction of the parasite into New Orleans probably occurred after 1965 since the parasite was not found in rats examined in 1965. Twenty years later, however, it was found.

It is inconsequential, however, that the parasite is endemic in the Western Hemisphere but it is of great concern on how far it will spread and will it be responsible for more CNS disease in humans and in animals.

REFERENCES

Aguiar DH, Morena P, Pascual J. First record of *Angiostrongylus cantonensis* in Cuba. *Am J Trop Med Hyg* 1981;30:963-5.

Aguilar RF, Topham K, Heatley JJ, *et al*. Neural angiostrongylosis in non-human primates: diagnosis, treatment and control of an outbreak in Southern Louisiana. *Proc Am Assoc Zoo Vet* 1999: 272-6.

Alicata JE, Jindrak K. Angiostrongylus in the Pacific and Southeast Asia. Springfield Ill: CC Thomas, 1970:105pp.

Andersen E, Gubler DJ, Sorensen K, *et al*. First report of *Angiostrongylus cantonensis* in Puerto Rico. *Am J Trop Med Hyg* 1986; 35: 319-22.

Barrow KO, St Rose A, Lindo JF. Eosinophilic meningitis. Is *Angiostrongylus cantonensis* endemic in Jamaica. *WI Med J* 1996;45:70-1.

Cross JH. Public health importance of *Angiostrongylus cantonensis* and its relatives. *Parasitol Today* 1987;3:367-9.

Cross JH, Chi JHC. ELISA for the detection of *Angiostrongylus cantonensis* antibodies in patients with eosinophilic meningitis. *Southeast Asian J Trop Med Public Health* 1982;13:73-7.

Costa L RR, McClare JJ, Snider III TG, *et al*. Verminous meningoencephephomyelitis by *Angiostrongylus cantonensis* in an American miniature horse. *Equ Vet Edu* 2000;12:2-6.

Chen HT. Un nouveau nématode pulmonaire, *Pulmonena cantonensis n.g. n.sp,* des rats de canton. *Ann Parasitol* 1935;13:312.

Campbell BG, Little MD. The finding of *Angiostrongylus cantonensis* in rats in New Orleans. *Am J Trop Med Hyg* 1988;38:568-73.

Cadilla JS, Almuedo Paz A, Fernandez de Mera JS, *et al*. Meningoencefalomielitis por *Angiostrongylus cantonensis* con afectacion pulmonary. *An Esp Pediatr* 1998;49:308-10.

Dougherty EC. The genus *Angiostrongylus* Cameron 1927 (Nematode: *Metastrongylidae*) and its relatives with description of *Parafilaroides* gen. nov., *Angiostrongylus gubernaculatus,* sp. nov. *Proc Helm Soc Wash* 1946;13:16-26.

Dorta-Contreras AJ, Reiber H. Intrathecal synthesis of immunoglobulins in eosinophilic meningitis due to *Angiostrongylus cantonensis*. *Clin Diag Lab Immunol* 1998;5:452-5.

Eamsobhana P, Dechkum N. Recognition of a 31–kDa diagnostic antigen from excretory/ secretory products of adult *Parastrongylus cantonensis* by infected human sera. *Trop Biomed* 2000;17:103-8.

Gardiner CH, Wells S, Gutter L, *et al*. Eosinophilic meningoencephalitis due to *Angiostrongyliasis cantonensis* as the cause of death in captive non-human primates. *Am J Trop Med Hyg* 1990;42:70-4.

Hwang KP, Chen ER. Clinical studies on Angiostrongyliasis among children on Taiwan. *Southeast Asian J Trop Med Public Health* 1991;(suppl);22:194-9.

Kliks MM, Palumbo NE. Eosinophilic meningitis beyond the Pacific Basin: The global dispersal of a peridomestic zoonoses caused by *Angiostrongylus cantonensis*, the nematode lungworm of rats. *Soc Sci Med* 1992;34:199-212.

Kim DY, Stewart TB, Bauer RW, Mitchell, M. *Parastrongylus (Angiostrongylus) cantonensis* now endemic in Louisiana wildlife. *J Parositol* 2002;88:1024-6.

Lindo JF, Waugh C, Hall C, *et al*. Enzootic *Angiostrongylus cantonensis* in rats and snails after on outbreak of human eosinophilic meningitis, Jamaica. *Emerg Infect Dis* 2002;8:324-6.

Martinez-Delgado JF, Gonzalez-Cortinas M, Tapanes-Cruz FR, Ruiz-Mendez A. Meningoencefalitis eosinofilica en Villa Clara (Cuba) Estudio de 17 pacientes. *Rev Neurol* 2000;31:417-21.

Matsumoto T. On a nematode found in the lung, especially with the pulmonary artery of the wild rat. *J Med Assoc Formosa* 1937;36:2620-3.

Nomura S, Lin PH. First case report of human infection with *Haemostrongylus ratti*, Yokagawa. *Taiwan No Ikai* 1945;3:589-92.

New D, Little MD, Cross J. *Angiostrongylus cantonensis* infection from eating raw snails. *N Engl J Med* 1995;332:1105-6.

Pascual JE, Bouli RP, Aguiar PH. Eosinophilic meningoencephalitis in Cuba caused by *Angiostrongylus cantonensis. Am J Trop Med Hyg* 1981;30:960-2.

Perera GM, Yong J, Rodriguez D, Galyez D. Cuban endemic molluscs infected with *Angiostrongylus cantonensis*. *Malacol Rev* 1983;16:87-8.

Raccurt LP, Blaise J, Durette-Desset MC. Presence d' *Angiostrongylus cantonensis* en Haiti. *Trop Med Int Health* 2003;8:423-6.

Slom TJ, Cortese MM, Gerber SI, *et al*. An outbreak of eosinophilic meningitis caused by *Angiostrongylus cantonensis* in travelers returning from the Caribbean. *N Engl J Med* 2002;346:668-75.

Teles HMS, Vaz JF, Fontes LR, Domingos MF. Registrode *Achatina fulica*, Bowdich, 1822 (Mollusca, Gastropoda) no Brazil: caramujo hospedeiro intermediario da angiostrongiliose. *Rev Sau Pub* 1997;3:310-2.

Ubelaker, JE. Systematics of species referred to the genus *Angiostrongylus. J Parasitol* 1986;72:237-44.

Vargus M, Gomez Perez JD, Malek E. First report of *Angiostrongylus cantonensis* (Chen 1935) (Nematoda; Metastrongylidae) in the Dominican Republic. *Trop Med Parasitol* 1992;43:253-5.

Vasconellos MC, Pike E. Occurrence of *Achitina fulica* in the Vale do Paroiba, Rio de Janiero State, Brazil. *Rev Sau Pub* 2001;35:585-4.

Yokogawa S. A new species of nematode found in the lung of rats, *Haemostrongylus ratti*: sp. nov. *Trans Nat Hist Soc Formosa* 1937;27:247-50.