Human angiostrongyliasis

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Human angiostrongyliasis caused by *Angiostrongylus cantonensis*, a rat lungworm, has been reported globally. Human infections are acquired by ingestion of raw or undercooked snails or slugs, paratenic hosts such as prawns, or contaminated vegetables that contain the infective larvae of the worm. So far, at least 2827 cases of the disease have been documented worldwide. During the past few years, several outbreaks of human angiostrongyliasis have been reported in mainland China, Taiwan, and the USA. Additionally, sporadic cases in travellers who have returned from endemic areas have been reported. We review the clinical features, diagnosis, and treatment of human angiostrongyliasis, and describe the geographical distribution and prevalence of *A cantonensis*. Educating the public about the dangers of eating raw or undercooked intermediate and paratenic hosts in endemic areas is essential for the prevention and control of this foodborne zoonotic disease.

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Introduction

The nematode worm *Angiostrongylus cantonensis* was discovered in the pulmonary arteries and hearts of domestic rats in Guangzhou (Canton), China, by Chen in 1935.[1] *A cantonensis* is a zoonotic pathogen, which occasionally causes human angiostrongyliasis with the main clinical manifestation of eosinophilic meningitis. The first human case of angiostrongyliasis was reported in Taiwan in 1945.[2] Since then, several outbreaks of the disease in human beings have been reported in the Pacific islands,[2,3] and, so far, more than 2800 cases have been documented worldwide. In the past 10 years, several major outbreaks of the disease have been reported in endemic regions, especially in China (nine outbreaks in mainland China and three in Taiwan). Additionally, a growing number of travellers have been diagnosed with eosinophilic meningitis caused by *A cantonensis* after returning from endemic regions.[4–11] These recent outbreaks have caused great concern for both the general public and physicians.

Aetiology and pathology

A cantonensis, a rat lungworm, is endemic in south Asia, the Pacific islands, Australia, and the Caribbean islands. The life cycle of this nematode involves rats as the definitive host, molluscs as intermediate hosts, and crustaceans (prawns and land crabs), predacious land planarians (flatworms in the genus *Platydemus*), frogs, and monitor lizards as paratenic (transfer or transport) hosts (figure 1). Human beings acquire *A cantonensis* after eating intermediate or paratenic hosts, or vegetables that contain the infective larvae (the third stage) of the worm (figure 1). Once swallowed, the infective larvae are digested from those vectors and invade intestinal tissue, causing human enteritis, before passing through the liver.[19] Cough, rhinorrhoea, sore throat, malaise, and fever can develop when the worms move through the lungs.[20] Finally, the larvae reach the central nervous system in about 2 weeks and eosinophilic meningitis and eosinophilic pleocytosis ensue.

The major pathological changes of human angiostrongyliasis occur in the brain.[21–23] According to autopsy studies, the external surface and spinal cord are

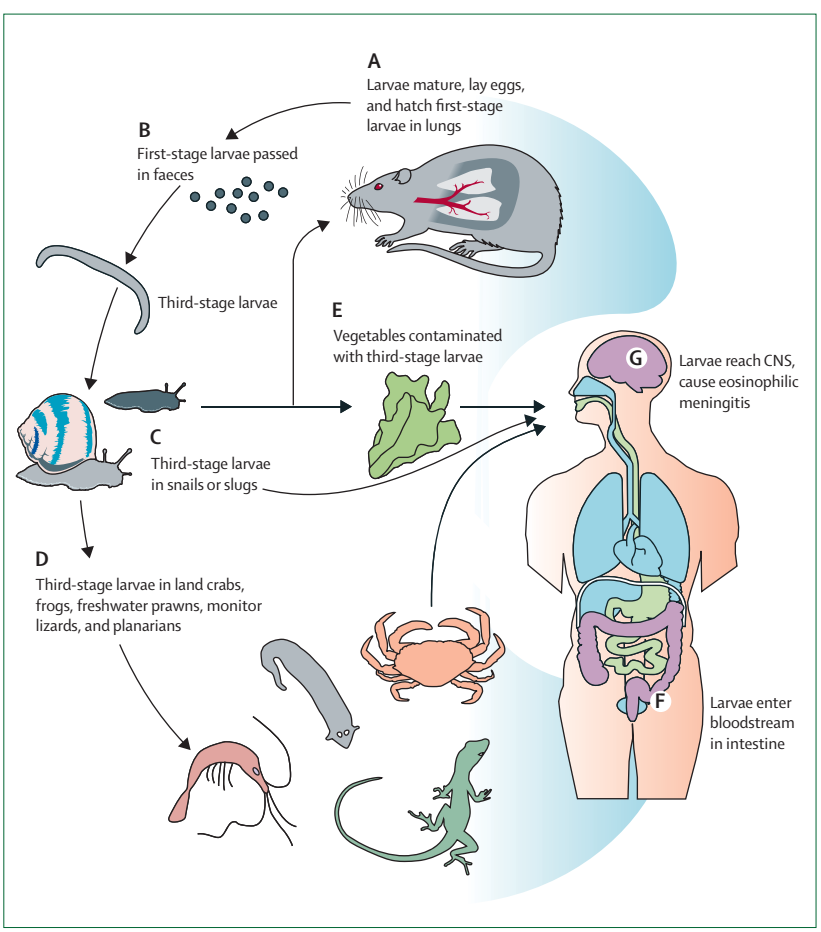

Figure 1*: The life cycle of *A cantonensis
Rats, as definitive hosts, acquire *A cantonensis* when the third-stage larvae are ingested. The larvae enter the bloodstream and reach the central nervous system (CNS), where they moult twice to become adult worms in 2 weeks.[12] The adult worms migrate to the pulmonary arteries and develop to sexual maturity and lay eggs (A). An adult female nematode produces around 15 000 eggs daily.[13] Eggs are carried to the capillaries and break into the air spaces where they hatch. The first-stage larvae (the juveniles) migrate up the trachea and are swallowed, and are excreted out with the faeces (B). Approximately 6–8 weeks after infection, the rat excretes the first-stage larvae.[13] The larvae in faeces are swallowed by intermediate host molluscs (snails or slugs) and develop into third-stage (infective) larvae in 12 days (C).[14] The third-stage larvae are then transmitted to the paratenic hosts such as shrimps, land crabs, predacious land planarians, and monitor lizards (D).[15–18] Human beings occasionally acquire *A cantonensis* when they eat snails, slugs, and sometimes, land crabs, frogs, freshwater shrimps, monitor lizards, or vegetables, which contain the infective larvae (E). The larvae are digested from tissues and enter the bloodstream in the intestine (F). The larvae finally reach the CNS and cause eosinophilic meningitis (G) or move to the eye chamber and cause ocular angiostrongyliasis.

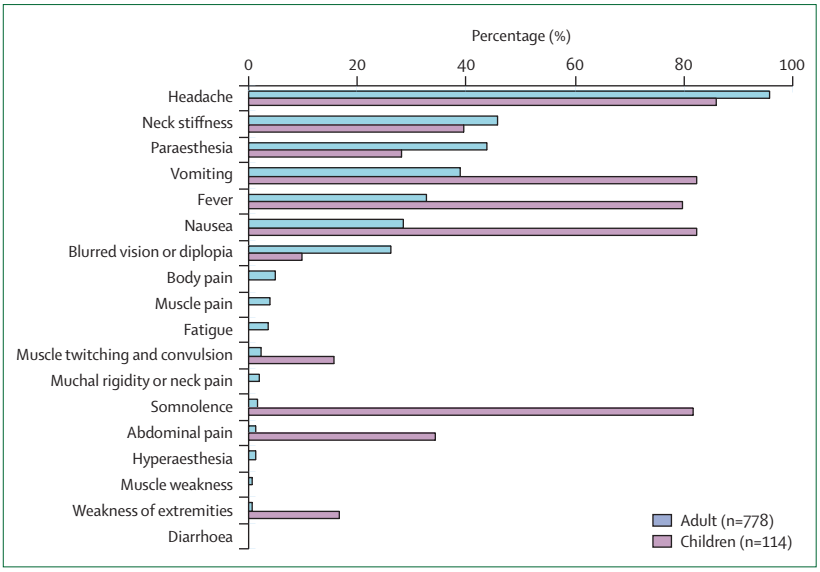

***Figure 2*: Clinical symptoms and signs of human angiostrongyliasis with eosinophilic meningitis**
Data are summarised from references reported in Thailand, Taiwan, mainland China, and the USA.[11,19,24,26,27,31–38]

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generally normal and gross haemorrhage is not commonly seen. Infiltration of lymphocytes, plasma cells, and eosinophils is commonly reported in the meninges and around intracerebral vessels.[21,23] Cellular infiltration around living worms is not prominent, but dead worms were usually surrounded by a granuloma, an increase in the number of eosinophils, and sometimes Charcot-Leyden crystals.[21] The physical lesions of tracks and microcavities caused by movement of the worms can be found in the brain and even in the spinal cord. The larvae can also move to the eyes and cause ocular angiostrongyliasis with visual disturbance such as diplopia or strabismus in many patients.[24,25]

Clinical features

The term human angiostrongyliasis refers primarily to eosinophilic meningitis/meningoencephalitis, the major clinical feature of *A cantonensis* infection in human beings. The incubation of this disease is highly variable, ranging from 1 day to several months, depending on the number of parasites involved.[19,26–29] In an outbreak in Beijing, China, the incubation period of 128 (80%) of 160 patients was 7–35 days.[30] In an outbreak in Wenzhou, Zhejiang, China, clinical symptoms appeared in 40 (62%) of 65 patients on days 6–15 after infection.[31]

Figure 2 summarises the clinical symptoms reported in 778 adult and 114 paediatric patients with eosinophilic meningitis caused by *A cantonensis*.[11,19,24,26,27,31–38] In adult patients, the common symptoms were headache (95%), neck stiffness (46%), paraesthesia (44%), vomiting (38%), and nausea (28%). Headache, mainly caused by increased intracranial pressure or the direct damage of the larvae, was intermittent, frequent, and severe at first; after repeated lumbar puncture, it became less frequent and less severe, and eventually resolved.[19,24] Neck stiffness was usually mild and lasted for a short period. Nuchal rigidity was less common, but has been reported in severe cases.[11,39] Paraesthesia, which usually persisted for less than 2 weeks and occurred in a variety of anatomical locations (usually in the extremities) was expressed as pain, numbness, itching, or a sensation of worms crawling under the skin.[19] Vomiting and nausea were probably related to increased intracranial pressure and usually disappeared after the first lumbar puncture. Although few adult patients with visual disturbance or diplopia were reported in China, this symptom was noted in 184 (38%) of 484 patients in Thailand and 11 (92%) of 12 patients in the USA.[11,24] 32% of adult patients had fever, which was mostly low grade; however, approximately 10% of these had high-grade fever ranging from 38°C to 39°C.[19,24]

In children, stiff neck and paraesthesia were less common than in adult patients, whereas reports of nausea and vomiting were higher. Of 94 (82%) paediatric patients with nausea and vomiting, 56% had projectile vomiting, which usually disappeared within 1 week.[19] Additionally, rates of fever, somnolence, constipation (76%), and abdominal pain were higher in children than in adults. In adults or children with heavy infections, coma and death can occur.[19,22]

***Panel*: Differential diagnosis of eosinophilic meningitis[41]**

Infectious causes
- *Angiostrongylus cantonensis*
- *Gnathostoma spinigerum*
- *Paragonimus* spp
- *Strongyloides stercoralis*
- *Toxocara canis*
- *Loa Loa*
- *Toxoplasma gondii*
- *Taenia solium*
- *Coccidioides immitis*
- *Schistosoma japonicum*
- *Fasciola hepatica*
- *Trichinella spiralis*

Non-infectious causes
- Malignant tumours
  - Glioblastoma
  - Hodgkin's disease
  - Non-Hodgkin lymphoma
  - Acute leukaemia
  - Meningeal carcinomatosis
- Drugs
  - Post myelography
  - Ibuprofen
  - Ciprofloxacin
  - Vancomycin
  - Gentamicin
- Foreign bodies
  - Ventriculoperitoneal shunts
- Primary eosinophilic meningitis

Diagnosis and treatment

The recovery of *A cantonensis* from cerebrospinal fluid or the ocular chamber confirms human angiostrongyliasis. However, the frequency of detecting these worms in patients is very low. Worms were only recovered from 28 (11%) of 259 human cases in Taiwan, and only ten (2%) of 484 human cases in Thailand.[19,24] Presumptive diagnosis of human angiostrongyliasis can be based on clinical symptoms, medical history, laboratory findings in blood and cerebrospinal fluid, brain imaging results, and serological tests. A history of eating intermediate or paratenic hosts is crucial for diagnosis of *A cantonensis* infection.

Eosinophils have an important role in the innate resistance of human beings to *A cantonensis* infection.[40] During infection, the proportion of eosinophils can reach to at least 10% of the white blood cell count (100–1000 eosinophils per µL) in cerebrospinal fluid (normal range <10 eosinophils per µL),[11,19,34,36] and 7–36% of the white blood cell count in peripheral blood (normal range 0·5–5%).[34] In human angiostrongyliasis, the cerebrospinal fluid has been reported as either turbid or clear.[34] The protein concentration in the cerebrospinal fluid from patients infected with *A cantonensis* is usually slightly raised, whereas glucose concentration is frequently lower than the normal range.

However, other causes for eosinophilic meningitis must be considered and ruled out before human angiostrongyliasis can be presumed (panel). MRI and CT have been used to reveal lesions in the central nervous system and can be useful for the differential diagnosis of the disease from other parasitic diseases, such as cysticercosis, paragonimiasis, gnathostomiasis, and schistosomiasis.[19,39,41–45] MRI findings include abnormal enhancing lesions in the brain, especially hyperintense T2 signal lesions, which are different from the haemorrhagic lesions in *Gnathostoma spinigerum* infections.[45,46] CT scan of the brain can be normal or can show non-specific findings, including cerebral oedema, ventricular dilatation, and diffuse

	Number of patients treated (ages*)	Treatment	Outcome
Chen et al (2006)[26]	22 (adults 15–43 years)	Albendazole 400–1200 mg per day with dexamethasone 10–20 mg per day for 10–20 days	All patients recovered, serious side-effects were not detected
	Nine (adults 15–43 years old)	Praziquantel 400–1200 mg with dexamethasone 10–20 mg per day for 10–20 days	All patients recovered, serious side-effects were not detected
Han et al (2006)[27]	28 (adults 25–63 years old)	Albendazole 15–20 mg per day with dexamethasone 10 mg per day for 9–27 days	All patients recovered, serious side-effects were not detected, two recurred in a month
Tsai et al (2004)[33]	Five (adults 30–57 years old)	Dexamethasone 15 mg per day for 7 days, prednisolone 60 mg per day for another 7 days	All patients recovered in 3 weeks, but two cases had side-effects
Tsai et al (2001)[64]	Eight (adults 23–39 years old)	Mebendazole 200 mg per day with dexamethasone and prednisolone for 4–11 days	All patients recovered
Chotmongkol et al (2006)[65]	41 (adults 15 years old or over)	Mebendazole 10 mg/kg per day with prednisolone 60 mg per day for 14 days	Median duration of headache was 3 days; 8% had headache; no serious side-effects
Jitpimolmard et al (2007)[66]	34 (adults 15 years old or over)	Albendazole 15 mg/kg per day	Mean duration of headache was 8·9 days; 21% of headaches persisted; no serious side-effects
	32 (adults 15 years old or over)	Placebo	Mean duration of headache was 16·2 days
Chotmongkol et al (2004)[67]	26 (adults 15 years old or over)	Albendazole 15 mg/kg per day with prednisolone 60 mg per day for 14 days	Median duration of headache was 4 days; 12% had headache; no serious side-effects
	32 (adults 15 years old or over)	Placebo	Mean duration of headache was 8·9 days; 41% had persistent headache; no serious side-effects
Chotmongkol et al (2000)[68]	55 (adults 15 years old or over)	Albendazole 15 mg/kg per day for 14 days	Mean duration of headache was 5 days, 9% of cases had persistent headache; no serious adverse effects
	55 (adults 15 years old or over)	No drug treatment	Mean duration of headache was 13 days; 45% cases had persistent headache
Punyagupta et al (1970)[29]	284†	Analgesic for 14 days	35% patients had headache relief
	96†	Analgesic with prednisone 30–60 mg per day for 14 days	26% patients had headache relief
	56†	Penicillin 3·0–4·5 g or tetracycline 2 g per day for 14 days	34% of patients had headache relief
Slom et al (2002)[11]	Nine (adults 21–28 years old)	Analgesic with or without non-steroidal anti-inflammatory agents	All patients recovered, 67% had headache for at least 4 weeks
	Three (adults 21–28 years old)	Corticosteroid	Symptoms were markedly improved

*No information regarding treatment in children was found in the published case series we reviewed. †The ages of these patients were not defined in the study. However, 82% of the patients were older than 20 years.

Table 1: **Treatment for human angiostrongyliasis and its effectiveness**

	Cases (%)
Thailand[22,24,25,55,69–78]	1337 (47·33)
China (including Taiwan and Hong Kong)[19,26–28,30,33–35,38,46,52,79–96]	769 (27·22)
Tahiti, French Polynesia[2,97]	256 (9·06)
USA[3,6–8,11,36,37,98–101]	116 (4·11)
Cuba[42,102–104]	114 (4·04)
New Caledonia[100,105]	72 (2·55)
Japan[57,106–111]	63 (2·23)
Australia[100,112–116]	24 (0·85)
Vanuatu[59]	19 (0·67)
India[17,60,61,100,117,118]	10 (0·35)
Vietnam[39,100,119]	8 (0·28)
Malaysia[100]	6 (0·21)
Mayotte[100,120]	6 (0·21)
Réunion island, France[100]	4 (0·14)
Egypt[121]	3 (0·11)
Sri Lanka[122–124]	3 (0·11)
Cambodia[100]	2 (0·07)
Samoa[100]	2 (0·07)
Fiji[125]	2 (0·07)
Belgium[9]	1 (0·04)
Costa Rica[126]	1 (0·04)
Germany[127]	1 (0·04)
Indonesia[62]	1 (0·04)
Jamaica[128]	1 (0·04)
Italy[5]	1 (0·04)
Côte d'Ivoire[100]	1 (0·04)
New Zealand[129]	1 (0·04)
Papua New Guinea[100]	1 (0·04)
Switzerland[4]	1 (0·04)
UK[10]	1 (0·04)
Total	2827

Table 2: **Cases of human angiostrongyliasis reported in countries or regions**

meningeal enhancing ring or disc lesions, resembling a tuberculoma.[39,46,47]

Human antibodies IgA, IgM, IgG, and IgE to *A cantonensis* can be generated after infection.[48] Serological tests including ELISA have been developed to detect the antigens of or antibodies against *A cantonensis* in serum or cerebrospinal fluid. Various ELISA methods have been developed and have been shown to be effective, although none are commercially available.[49–52] A dot-blot ELISA using blood dried on filter paper has proven to be convenient for handling field samples for epidemiological surveys.[49] The sensitivity and specificity of this method were both 100% in laboratory diagnosis.[49] Several specific *A cantonensis* antigens, such as 29 kD, 31 kD, and 32 kD, have been identified for immunodiagnosis.[53–55] The 29 kD antigen from female *A cantonensis* worms has the potential to be a good marker for diagnosis. The sensitivity and specificity to detect human serum IgG4 were 75% and 95%, respectively.[56] Additionally, antigens from *A cantonensis* can also be detected in serum by immuno-PCR.[57]

Most cases of human angiostrongyliasis are mild and self-limiting, but death can occur in severe cases without prompt and proper treatment.[19,22,58,59] Surgery is required to remove worms from the eyes of patients with ocular angiostrongyliasis.[10,25,60–62] For eosinophilic meningitis, lumbar puncture should be done to relieve headache caused by increasing intracranial pressure.[19,24] Treatment is supportive and symptomatic using analgesics with or without corticosteroids.[19,24]

Anthelmintic drugs, such as albendazole and mebendazole, are usually not recommended for treatment of *A cantonensis* infections, because of the possibility of exacerbating neurological symptoms.[63] However, these compounds have been used to treat the disease effectively in mainland China, Taiwan, and Thailand (table 1). Indeed, anthelmintic drugs can relieve symptoms and reduce the duration of the disease. For example, the symptoms and signs of acute angiostrongyliasis were rapidly relieved in the first 3–6 days of treatment in eight patients given 20 mg/kg of albendazole daily for 9 days.[27] In Thailand, the mean duration of headache was reduced substantially by use of albendazole alone.[66,68] Corticosteroid therapy was shown to be effective in treating *A cantonensis* infections in Thailand. Symptomatic headache caused by eosinophilic meningitis was relieved in patients who received a 2-week course of prednisolone (60 mg per day).[65] In China, the combination of corticosteroids and anthelmintics has been commonly used to treat human angiostrongyliasis. 28 patients were given albendazole 15–20 mg/kg per day in combination with dexamethasone 10 mg per day for 9–27 days. All patients recovered without sequelae.[27] Similar therapy was also used in 31 patients given albendazole or praziquantel (400–1200 mg) in combination with dexamethasone (10–20 mg) daily for 10–20 days. 29 patients recovered completely within a month. Two patients developed recurrence, but recovered after being treated again with the same regimen.[26]

Epidemiology

Human angiostrongyliasis worldwide

Since the first case of human angiostrongyliasis was reported in 1945, more than 2800 cases have been reported in approximately 30 countries (table 2). However, many cases could have gone unreported or unrecognised during the past decades.[100] Human angiostrongyliasis frequently occurs in outbreaks with case numbers ranging from tens to hundreds. In these outbreaks, people usually become infected by eating raw or undercooked food containing or contaminated with the larvae of *A cantonensis*. In 1961, an outbreak of several hundred cases of eosinophilic meningitis, attributed to *A cantonensis,* was reported in Tahiti, French Polynesia.[2]

Since the initial confirmation of two cases of eosinophilic meningitis caused by *A cantonensis* in Hawaii in 1962,[13] the parasite has been found as the cause of many

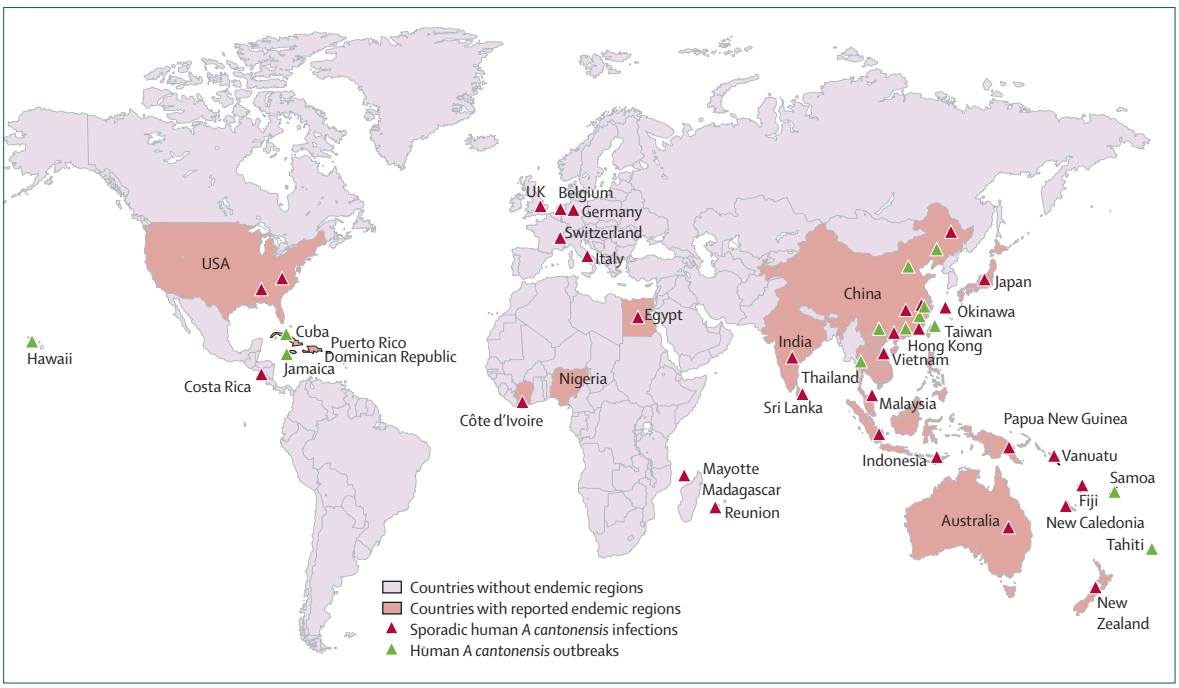

***Figure 3*: Distribution of *A cantonensis* and human *A cantonensis* infections or outbreaks worldwide**
Endemic regions are those countries in which human cases of angiostrongyliasis or animal reservoirs of *A cantonensis* have been identified. This is not intended to imply that *A cantonensis* is endemic throughout these entire countries. Conversely, those areas marked as non-endemic regions may well be countries where no investigation has taken place and so cannot be considered free from *A cantonensis* infection.

other cases in the Pacific islands and south Asia. *A cantonensis* is mainly endemic in these regions; however, endemic regions have now extended beyond the Pacific islands and south Asia, perhaps as a result of the unintended importation of definitive rodent hosts on ships and aeroplanes (figure 3). The Caribbean islands—where the first case of human angiostrongyliasis was reported in Cuba in 1973[103]—have reported increasing numbers of human *A cantonensis* infection, with several cases reported in Costa Rica and Jamaica.[11,126,128] Of a group of 23 US travellers, 12 developed eosinophilic meningitis after returning from Jamaica in 2000.[11] Additionally, other sporadic cases of human *A cantonensis* infection have been described in travellers after returning from the Pacific or Caribbean islands.[4–11]

At least 1337 cases of human angiostrongyliasis have been reported in Thailand. The high rate of the disease in the Thai population is linked to the custom of eating raw or undercooked snails (*Pila* spp) with alcohol, which is especially popular among young adult men.[18,74] About 75% of human angiostrongyliasis cases around the world have occurred in adults (figure 4). 70% of Thai patients infected with *A cantonensis* were 20–40 years old.[24] By contrast, 65% of the reported 125 cases in Taiwan have been in children less than 10 years of age.[19]

In mainland China, the first case of human angiostrongyliasis with eosinophilic meningitis was reported in 1984 in Guangdong province. Only a few additional cases were recorded from this region before 1997.

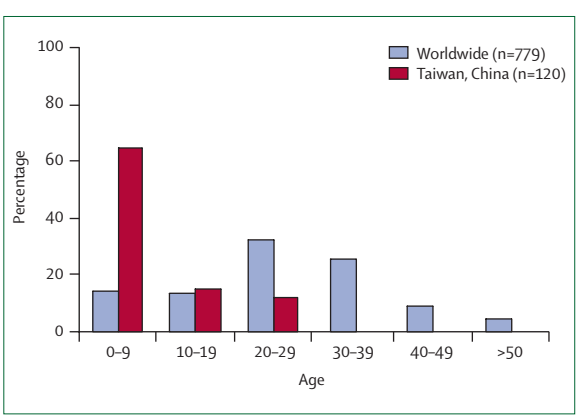

***Figure 4*: Ages of patients who have acquired angiostrongyliasis**
Data are summarised from references 3, 11, 19, 28, 29, 36, and 111. Although 125 cases of *A cantonensis* were reported in Taiwan, the exact ages of five patients were not recorded, and are therefore not shown in this figure.

Outbreaks of human infection with *A cantonensis* have been reported with increasing frequency in mainland China in recent years, possibly caused by the growing popularity of eating exotic foods such as raw and undercooked snails. One outbreak of human *A cantonensis* infection with 65 cases of eosinophilic meningitis was observed in Wenzhou, Zhejiang province, in 1997.[28] An outbreak of five human cases occurred in Liaoning province in 1999,[81] and three outbreaks with a total of 30 cases were reported in Fujian province in 2002.[35,38,85] Two

	Number of rats examined	Number of rats with *A cantonensis* infection (%)
Rattus norvegicus		
Guangzhou, China (2005)[13,81]	21 375	363 (2)
Fujian, China (2001)[13,81]	391	38 (10)
Zhejiang, China (2000)[13,81]	351	72 (21)
Taiwan (1957–62)[13,81]	328	26 (8)
New Orleans, USA (1986–87)[133]	94	20 (21)
Indonesia (1978)[134]	98	13 (13)
Queensland, Australia (1980)[135]	77	8 (10)
Thailand (1995)[136]	58	2 (4)
Philippines (1965)[137]	51	2 (4)
Jamaica (2000)[138]	35	4 (11)
Cuba (1981)[139]	20	12 (60)
Haiti (2003)[140]	19	4 (21)
Papua New Guinea (1984)[141]	7	1 (14)
Dominican Republic[142]	5	5 (100)
Rattus rattus		
Taiwan (1957–62)[13,81]	792	26 (3)
Queensland, Australia (1980)[135]	174	37 (21)
Yoron Island, Japan (1979–82)[143]	108	30 (28)
Jamaica (2000)[138]	74	20 (27)
Fiji (1984)[144]	54	16 (30)
Thailand (1995)[136]	22	17 (77)
Thailand (1997)[136]	16	16 (100)
Haiti (2003)[140]	4	3 (75)
Rattus exulans		
Fiji (1984)[144]	42	25 (60)
Indonesia (1978)[134]	14	4 (29)

Table 3: **Primary definitive hosts of *A cantonensis* in severely endemic regions**

outbreaks with 59 human cases occurred in Yunnan province in 2005 and 2006.[26,27] Unfortunately, these outbreaks do not seem to have drawn sufficient public attention to the threat of this parasite in China, a situation that contributed to a larger outbreak of some 160 cases in Beijing in 2006.[30]

So far, *A cantonensis* in animal reservoirs has been reported from at least ten provinces in mainland China, where more than 650 million people are estimated to be at risk. Epidemiological surveys indicate that most patients in these outbreaks had eaten raw or undercooked meat of an invasive freshwater snail, *Pomacea canaliculata*, before becoming sick. The same exposure pattern was also reported in two outbreaks with a total of 17 human infections in Taiwan in 1998 and 2001.[34,64] *P canaliculata*, which is native to South America, was imported into Taiwan in 1981 as a food source,[64] and then introduced to mainland China.[130] It has replaced the African giant snail, *Achatina fulica*, as the major intermediate host of *A cantonensis* and has become the main source of human infection in Taiwan and mainland China.[130]

Hosts for *A cantonensis* and their role as reservoirs of infection

Most species of molluscs are susceptible to and capable of transmitting *A cantonensis*. Terrestrial and some aquatic snails are the primary intermediate hosts.[18,131] However, in certain regions, one or two species of snails or slugs are the main intermediate hosts and the intensity of infection in these hosts is usually very high. For example, the giant African snail *Ac fulica* is the major source of infection worldwide. The dispersal of *A cantonensis* was associated with the spread of this snail from its native origin in Africa throughout the Pacific islands and south Asia.[100] The golden apple snail *P canaliculata* has a wide distribution in Asia and has caused great damage to local agricultural systems. Unfortunately, this snail is also very susceptible to *A cantonensis* and has become an important intermediate host in these regions.[130] The infection rate in *P canaliculata* is very high—21% in Taiwan, 42–69% in mainland China, and 10–39% in Okinawa, Japan. In Thailand, *Pila* spp snails are frequently eaten by men, thus causing human infection. However, since *Pila* spp are poor vectors and contain less infective *A cantonensis*,[18] human infections have milder clinical signs than those caused by eating *P canaliculata*.

There is little knowledge regarding the prevalence of *A cantonensis* in reported paratenic hosts.[15,17,63] Small planarians could represent a very important but overlooked source of human infection when they are consumed together with contaminated uncooked vegetables. Four outbreaks of human angiostrongyliasis have been caused by eating contaminated vegetables or vegetable juice.[11,33,59] An outbreak with five cases in Taiwan linked to drinking vegetable juices occurred in 2001.[33]

In New Caledonia, 53% of frogs (*Hyla aurea*) were found to contain the infective larvae.[132] Eating raw frogs has been implicated in human infections in Taiwan, mainland China, and the USA. In Thailand, 21 (95%) of 22 monitor lizards studied were found to be infected with *A cantonensis* and more than 18 cases of human angiostrongyliasis in Thailand, Sri Lanka, and India were attributed to consumption of monitor lizards.[15,17,63]

Rattus rattus and *Rattus norvegicus* have been considered the most common definitive hosts for *A cantonensis*, but other species of rats found in rural and forested areas are also reported to be natural hosts.[13,18] Rats are necessary for the establishment of *A cantonensis* foci in an area. When *A cantonensis* is identified in rats, the parasite is deemed to be endemic in that region. Table 3 summarises the prevalence of *A cantonensis* in definitive hosts in regions where human infections or outbreaks have occurred. The infection rates in *R norvegicus*, the primary definitive host, are highly variable.

Human beings and non-human primates can be accidental hosts for *A cantonensis*, but the parasite is unable to complete its development and usually dies in

Search strategy and selection criteria

Data for this Review were identified by searches of Medline (PubMed), ScienceDirect, Highwire, JSTOR, Google scholar, and ISI Web of Knowledge. Search terms included "*Angiostrongylus cantonensis*", "*Parastrongylus cantonensis*", "*Angiostrongylus cantonensis* infection", "*Parastrongylus cantonensis* infection", "human *Angiostrongylus cantonensis* infection", "angiostrongyliasis", "human angiostrongyliasis", "Guangzhou guangyuanxianchong" [*A cantonensis*], and "Guangzhouguangyuanxianchongbing" [human angiostrongyliasis]. Relevant articles or book chapters in English and Chinese were consulted. These databases were searched up until 2007 when this Review was prepared. During the revision of this manuscript, additional citations brought to our attention were added.

the central nervous system, causing eosinophilic meningitis or even death. The worms have been reported as the cause of death of captive primates in the Bahamas, Australia, and the USA.[98,145–147]

Prevention and control

Because of the large number of rats and molluscs that are highly susceptible to *A cantonensis* worldwide, it would be very difficult to eradicate this parasite from the environment. However, it is possible to block the transmission pathway of *A cantonensis* to human beings by educating susceptible populations to avoid eating raw or undercooked intermediate and paratenic hosts or potentially contaminated vegetables. The habit of eating raw snails and paratenic hosts should be strongly discouraged, although it is often difficult for people to abandon customs that have existed for generations in endemic regions such as Thailand and China, where snails are a popular food and are prepared in various ways. For example, eating raw or undercooked snails with seasonings, such as pepper and pericarpium, is very popular in Chinese restaurants. Several outbreaks of human *A cantonensis* infections in China have been attributed to this method of preparing snails. So far, recommended measures for prevention of *A cantonensis* in endemic regions include: (1) educating the public to be aware of *A cantonensis* and the disease caused by this parasite; (2) only eating adequately cooked snails, slugs, small molluscs, and paratenic hosts of *A cantonensis* such as frogs, shrimps, land crabs, and monitor lizards; (3) eradicating molluscan hosts near houses and vegetable gardens; and (4) not eating unwashed vegetables that may be contaminated with the infective-stage larvae of *A cantonensis*. Travellers heading to endemic regions must be made aware of the dangers of eating raw molluscs and vegetables from unknown sources and should avoid these foods. Washing hands frequently, particularly after gardening, is also strongly recommended.

Programmes educating public-health workers and physicians in endemic areas about *A cantonensis* and its hosts is a practical and achievable intervention for the control of human infection. Human beings with clinical symptoms of severe headache, stiff neck, nausea, vomiting, and paraesthesia should be considered likely to be infected with *A cantonensis*, and parasitological and serological tests must be done to confirm or rule out the tentative diagnosis.

Conflicts of interest

We declare that we have no conflicts of interest.

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