

# Eosinophilic Meningoencephalitis Caused by the Rat Lung Worm, *Angiostrongylus Cantonensis* with Special Reference to *A. Malaysiensis* in Malaysia

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## Introduction

*ANGIOSTRONGYLUS CANTONENSIS* (Chen, 1935), a metastrongyle nematode (Protostrongylidae, Nematoda) found in the lungs of rats in Canton, China was described as *Pulmonema cantonensis*. Matsumoto (1937) found this worm in rats in Taiwan, and in the same year Yokogawa (1937) described it as *Hematostrongylus ratti*. Dougherty (1946) treated the genus *Pulmonema* as synonymous with *Angiostrongylus* (Kamenskii, 1905) and since then the worm is known as *A. cantonensis*.

## Geographical Distribution

*A. cantonensis* which is found in wild rats (definitive hosts) and molluscs (intermediate hosts) is widely distributed.

- a. *Southeast Asia* :- Philippines (Nishimura and Yogore, 1965); Vietnam (Do and Hendricks, 1974); Indonesia (Kwo and Kwo, 1968); Thailand (Harinasuta *et. al.* 1964; Crooks *et. al.* 1968); Malaysia (Schacher and Cheong 1960; Lim *et. al.* 1965; Lim and Heyneman, 1965; Lim, 1967, 1970; Lim and Ungku Omar-Ahmad, 1969).
- b. *Other countries* :- East Africa (Brygoo and Chabaud, 1964; Alicata, 1965); India (Parmeter and Chowdhury, 1966); Queensland, Australia (Mackerras and Sanders, 1955); Ryukyu Islands, Japan (Nishimura *et. al.* 1964); Taiwan (Kuntz and Myers, 1946); Pacific Tropics (Alicata 1963a; Wallace and Rosen, 1965).

## *Angiostrongylus cantonensis* in Man

Nomura and Lin (1945) reported the first human infection in Taiwan where the worm was found in the cerebro-spinal fluid of a patient having eosinophilic meningoencephalitis. Several cases of this disease were reported later (Hsieh, 1967; Chiu *et. al.* 1968). Rosen *et. al.* (1962) reported adult nematodes occurring in the brain of a man in Hawaii, and they were confirmed to be *A. cantonensis* (Chitwood, 1961). In Vietnam a fatal case of eosinophilic meningoencephalitis was reported in a girl of 18 years at Haiphong by Jindrak and Alicata (1965). From serial histological sections of the brain, the morphological characters of the nematodes are believed to be that of young adults of *A. cantonensis*. Tangchai *et. al.* 1967, reported *Angiostrongylus* probably *cantonensis* in the brain of a Thai woman who died of eosinophilic meningoencephalitis. In Malaysia two cases with worms found in the CSF were reported by Watts (1969) and Bisseru (1972).

Several cases of ocular angiostrongyliasis in Thailand were also reported (Promminderroj *et. al.* 1962; Ketsuwan and Pradatsundarsar, 1965, 1966).

## Clinical and Symptomatic Cases of Eosinophilic Meningoencephalitis

An epidemic of this disease occurred in Ponape, Eastern Carolines (Bailey, 1948). Further incidences were reported in the Pacific Tropics (Franco *et. al.* 1960; Allison, 1962), Vietnam (Sison *et. al.*). Indonesia (Smit, 1962), Thailand (Khwanmitra *et. al.* 1957; Punyadasni and Punyagupta, 1961; Tanti-behduangur, 1963; Behjapong, 1964; Punyagupta, 1965) and in Malaysia (Watts, 1969; Bisseru, 1972).

The epidemiology of this disease suggests that direct ingestion of certain food of animal origin was involved in the transmission of the parasite to man. In Thailand, Punyadasni and Punyagupta (1961) and Punyagupta (1965) discovered that eosinophilic meningoencephalitic patients had ingested pickled snails, *Pila ampullacea*. Naturally infected *Pila scutata* in Malaysia when consumed, could transmit the same disease (Lim and Krishnansamy, 1970). In the Pacific Tropics certain infected fresh water crustaceans (prawns), fish, land crabs, when eaten, transmitted the infective larvae of the parasite to man (Bailey 1948; Alicata and Brown, 1962; Rosen *et. al.* 1967; Franco *et. al.* 1960; Alicata 1965a). The African snail *Achatina fulica*, commonly eaten in certain parts of Taiwan (Formosa) has been implicated in several cases of cerebro-angiostrongyliasis (Hsieh, 1967). Heyneman and Lim (1967) found that fresh vegetables in Malaysia may be involved in the transmission of these parasites to man.

The parasite seldom reaches maturity in man, an accidental host, and in all but one positive case, the parasite were found only in the cerebrum, cerebellum or spinal cord. The exceptional case was a 5-year old female in South Taiwan who died of the disease; immature worms were recovered from the brain and spinal cord, but mature worms were found in the lungs (Chin *et. al.* 1968).

#### Clinical Manifestations of *A. Cantonensis*

The most typical symptoms of the disease start about two weeks after infection with an abrupt or slowly increasing headache, neck and back stiffness, photophobia, nausea and vomiting (Bailey 1948). Sometimes, a generalised or focal hyperaesthesia of skin or muscles appears with signs of paralysis of one or more nerves. The temperature may be slightly elevated. After one or two weeks duration, the symptoms slowly disappear.

The following symptoms are listed in accordance with frequency of their occurrence (Alicata and Jindrak, 1970).

- a. Headache with a throbbing syndrome is the most constant symptom of angiostrongyliasis.
- b. In most instances a headache is accompanied by nuchal and dorsal stiffness and pain.
- c. Photophobia often preceded or accompanied by blurring of vision.
- d. Vertigo, loss of balance on standing or sitting.
- e. Nausea, often followed by vomiting, accompanies other meningeal symptoms.
- f. Parthesiae consisting of sensations of burning, tingling, pain, numbness, commonly occur on the face, shoulders, forearm and trunk, sometimes over half of the body.
- g. Diplopia has been found in some cases.
- h. Defective hearing, troubles of deglutition and in articulation of speech have been found in some cases (Schollhammer *et. al.* 1966).
- i. Chills, malaise, anorexia, general aches and pains are manifestations of a more severe course of the disease.

Duration of the illness ranges from two to thirty-one days, but it may extend over several months (Bailey, 1948).

#### Angiostrongylus malaysiensis

Lim *et. al.* (1965) studied extensively the natural infections in field and house rats and various species of intermediate molluscan hosts with this parasite in different habitats throughout the country. In their studies of the adult worms slight difference were found in morphology between the Malaysian strain of *A. cantonensis* and the parasite in the original description by Chen (1935) and by Mackerras and Sanders (1955). Evidence of strain specificity among three geographical strains of *A. cantonensis*, namely the Thai, Hawaiian and Malaysian strains has been observed by Heyneman and Lim (1967) and by Lim and Heyneman (1968). These studies showed that previously infected rats developed no marked protection against heterologous strains, and that there was a high probability that the host was protected against a challenge by the homologous strain. Cross and Fresh (1969) demonstrated that the Malaysian strain could cause a different pathology in animals from that caused by the Thai and Hawaiian strains. Subsequently, the Malaysian strain, *A. cantonensis* was redescribed as a new species, *A. malaysiensis* by Bhaibulaya and Cross (1971). In view of the redescription of the parasite, Lim (1973) reexamined the *Angiostrongylus* adult worms which were previously studied by Lim *et. al.* (1965) and agreed with Bhaibulaya and Cross (1971) that the worm is a new species, *A. malaysiensis*. However, Lim (1974) also found forest rats naturally infected with *A. malaysiensis* and he postulated that the parasite is indigenous to Malaysia.

Lim *et. al.* (1965), Lim and Heyneman (1965) and Lim (1967) found that *A. cantonensis* (= *A. malaysiensis*) is a widespread parasite of domestic, rural and forest rats. It is transmitted by various

land snails and slugs (Lim *et. al.* 1965; Lim and Heyneman 1965; Lim, 1970; Bisseru, 1971). Fresh water snails have also been found to be susceptible intermediate hosts (Lim *et. al.* 1965; Lim and Heyneman, 1965). The worms develop in the rats, and mature in the pulmonary arteries after migrating through the brain (Lim *et. al.* 1965).

### Malaysian Cases

The first five cases of eosinophilic meningoencephalitis in Malaysia were reported from Sarawak (Watts, 1969). The clinical picture was that of a subacute meningitis with eosinophilic pleocytosis. All five patients suffered headache, muscle pains, fever, vomiting, diplopia, neck stiffness, papilloedema and cranial nerve palsies. The duration of illness was from 23-24 days. Larvae supposedly identified as *A. cantonensis* were recovered from two of the five cases. All the cases were treated with Hetrazan (diethylcarbamazine) in a dosage of 6 mgms/kgm body weight daily for 21 days.

None of the cases reported ate raw molluscs or crustaceans. In one case a child of eleven months old was occasionally given unpeeled banana to eat. The African snail *Achatina fulica*, intermediate host of the parasite, was found in large numbers on the fruit and leaves of banana trees, and it was suspected that this case was infected from the contaminated skins of bananas. Studies of the intermediate hosts of the parasite in Sarawak by Lim (1970), shows that other land molluscs, a species of land snail, *Macrochlamys resplendens*, land slugs, *Microparmarion malayanus*, and *Laevicaulis alte*, and a species of freshwater molluscs, *Pila scutata*, are abundant. The molluscs except *P. scutata* are also commonly found in banana plantations (Lim, 1970). *M. malayanus* in particular, is found always attached to banana trees and leaves, and this snail has been established to shed larvae on lettuce leaves (Heyneman and Lim, 1967).

The sixth Malaysian case of eosinophilic meningoencephalitis was observed in Kuala Lumpur, Peninsular Malaysia (Bisseru *et. al.* 1972). The patient was found to show all the symptoms of the disease, and two larval nematodes were recovered from the CSF, one of them alive. Unfortunately no illustration of the two larval nematodes was given, but they have been allegedly identified by the authors as late third stage larvae of *A. cantonensis* corresponding to about the fifth post-infective day from the cerebrum of laboratory-bred white rats infected with the third stage infective larvae of the parasite. Measurements of the two worms were 0.52 mm long by 0.01 mm wide and 0.71 mm long by 0.01 mm wide. The mode of infection by the parasite in this case was suggested by the history

of the patient having eaten half cooked prawns, shellfish, raw lettuce, tomatoes and other salad greens contaminated by larvae.

In the Kuala Lumpur case, larvae reported as late third stage were recovered 17 days after the patient was known to have eaten a meal of half-cooked shellfish, prawns and raw vegetables Bisseru *et. al.* (1972). In monkeys (*Macaca mulatta*) fed with infective larvae of *A. cantonensis* 5th stage larvae developed in the brains 17 days after infection Weinstein *et. al.* (1973); these were found to be comparable to 5th stage larvae recovered from man after an infection of unknown duration Rosen *et. al.* (1962). Experimental study of local macaques (*M. fascicularis*) fed with infective larvae recovered from naturally infected slugs, *M. malayanus*, showed that some of the worms developed to 5th stage or sub-adult stage in the brains from 11 to 19 days after infection, but most of the other worms recovered were stunted Lim (1970). The normal worms consisted of nine 11 days, two 15 days, and four 19 days old. The mean measurement for the 11 days old worms was 1.94 mm (0.90-2.80) long and 0.05 mm (0.03-0.07) wide; for 15 days old, 2.29 mm (1.11-3.48) long and 0.07 mm (0.04-0.09) wide and for 19 days old 4.79 mm (3.57-5.88) long and 0.12 mm (0.08-0.14) wide. Mean measurement of 30 five days old worms recovered from experimental infected white rats was 0.64 mm (0.45-0.80) long and 0.01 mm (0.01-0.02) wide.

Epidemiologic evidence in these six instances of eosinophilic meningoencephalitis in Sarawak, and Kuala Lumpur suggests that ingestion of contaminated food with larvae of the parasite was the probable route of infection. Positive evidence for aetiological role of the parasite in three cases (Watts 1969; Bisseru 1971) was based on the finding of larvae in the cerebrospinal fluid. Since the larvae recovered from these cases were not available for further re-examination and as such one could question the authenticity of these cases.

### Conclusion

Six cases of human angiostrongyliasis have been reported in Malaysia up to the present time. Larvae, presumably *A. cantonensis*, were recovered in three of the six cases; the remaining four diagnoses were based on clinical signs and symptoms.

*Angiostrongylus malaysiensis* is widely distributed in Malaysia) in a number of land molluscs and rat host species (Lim *et. al.* 1965; Lim and Heyneman, 1965). Fortunately none of the land molluscs are consumable. Only two species of fresh water molluscs, *Pila scutata* and *Bellamyia ingallsiana*, were found to be edible (Lim and Krishnansamy,

1970). Of these *P. scutata* is found to be eaten by various communities in this country (Lim *te. al.* 1965; Lim 1970; Lim and Ungku Omar-Ahmad, 1969); thus there is a potential risk of human infection. The infection could also be acquired by eating foods, particularly raw vegetables, which are contaminated with the parasite shed by the land slug, *M. malayanus* and the African snail, *A. fulica* (Heyneman and Lim, 1967; Watts, 1969).

The freshwater snail, *P. scutata* is common in ricefields, fish ponds, and abandoned tin-miting pools. The land slug, *M. malayanus* and the African snail, *A. fulica* are abundant in vegetable gardens in the rural areas. It could appear that rural folks are more likely to come in contact with the parasite than people in the urban areas. Since the evidence for eosinophilic meningoencephalitis in Malaysia is inconclusive, a systematic survey of the rural folk for symptoms and signs of this disease – with special attention also to dietary habits – would be worthwhile.

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