AN OVERVIEW OF GNATHOSTOMIASIS IN THE WORLD

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Abstract. Gnathostomiasis is a typical fish-borne parasitic zoonosis. *Gnathostoma spinigerum* has long been considered the only species to cause human infection. Because of the distribution of this species and the eating habits of the people, gnathostomiasis was thought an unique parasitic disease in Asia, especially in Thailand and Japan. Around the 1970s, however, the presence of this disease was reported from Ecuador and Mexico, and now the endemicity in Latin America is considered the worst in the world. The causative species was recently proven to be *G. binucleatum*. In Japan, while gnathostomiasis due to *G. spinigerum* had almost disappeared by the 1970s, small outbreaks and/or sporadic cases caused by infection with *G. hispidum*, *G. doloresi*, and *G. nipponicum* were, one after another, discovered during the 1980s-1990s, suggesting that any *Gnathostoma* spp would cause human disease. Apart from those known endemics, an outbreak of gnathostomiasis among Korean emigrants in Yangon, Myanmar, was reported. Furthermore, collaborative study with Danish and Vietnamese parasitologists revealed that *G. spinigerum* infection is common in freshwater fishes in Vietnam, suggesting that gnathostomiasis would occur all over the Indochina peninsula. In fact, this expectation will be substantiated by the country report from Vietnam in this meeting. In addition to those known or predicted endemic areas, literature survey revealed that gnathostomiasis patients have been seen sporadically in Europe and North America. Those patients seen in non-endemic areas were mostly emigrants from endemic areas, but a few travelers from non-endemic areas also seemed to be infected during their travel to endemic areas. Gnathostomiasis has now become an important disease in travel medicine.

BIOLOGY OF THE GENUS *GNATHOSTOMA*

The genus *Gnathostoma* is a nematode parasite of carnivorous/omnivorous mammals. Till now, 13 species of the genus *Gnathostoma* have been identified with varying geographical distributions (Table 1; Daengsvang, 1980). Six species are found in Asia and seven in the Americas. Adult worms of the majority of *Gnathostoma* spp parasitize the stomach of the definitive hosts (*G. nipponicum* reside in the esophagus and some other species reside in the kidney or liver). They lay eggs in the feces of the definitive hosts and the first-stage larvae hatch from the eggs in freshwater. After being ingested by copepods (*Cyclops*), the first intermediate host, the larvae develop into early third-stage larvae. They are then ingested by freshwater fishes or amphibians, where they become advanced-third-stage larvae. Along with the food-chain, the advanced-third-stage larvae are distributed in a wide range of animals (paratenic hosts) including icthiophagous fishes, reptiles, birds, and rodents, without further development. When the second intermediate or paratenic hosts are ingested by the definitive hosts, they become adult worms to complete their life cycle (Fig 1). Although any second intermediate or paratenic host can be the source of human infection with *Gnathostoma* spp, the majority of patients have a history of ingesting raw or undercooked fish meat. Gnathostomiasis is, therefore, a typical fish-borne parasitic zoonosis. In Japan, a few cases were supposed to be infected by ingesting raw snake meat with a belief in its tonic effect (Kurokawa *et al*, 1998).

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GNATHOSTOMA AS A PATHOGEN OF HUMAN DISEASE

When the third-stage larvae are ingested by humans, they are unable to develop into the adult stage and migrate through human tissues, preferentially in the skin, to cause serpiginous eruption and/or mobile erythema. Although gnathostomiasis is generally known as cutaneous larva migrans, an accidental migration of the larvae into vital organs, such as the central nervous system (CNS) results in fatal or deleterious illness.

Among 13 species, only one *G. spinigerum*, had been known to cause human disease in Asian countries, especially Thailand and Japan (Daengsvang, 1980). However, since the 1980s, in Japan, *G. hispidum*, *G. nipponicum*, and *G. doloresi* were, one after another, proven to cause human disease (Nawa, 1991). In

Table 1
Currently accepted *Gnathostoma* species with reference to human infection.

Species	Natural definitive hosts	Habitat	Locality	Human infection
G. spinigerum Owen, 1836	feline, canine	stomach	Asia, Oceania	Yes
G. hispidum Fedtschenko, 1872	pig, wild pig	stomach	Asia, Europe	Yes
G. trugidum Stossich, 1902	opossum	stomach	Americas	
G. americanum Travassos, 1925	feline	stomach	South America	
G. doloresi Tubangui, 1925	pig, wild pig	stomach	Asia, Oceania	Yes
G. didelphis Chandler, 1932	opossum	liver	USA	
G. nipponicum Yamaguti, 1941	weasel	esophagus	Japan	Yes
G. procyonis Chandler, 1942	raccoon	stomach	USA	
G. brasiliense Ruiz, 1952	otter	liver	Brazil	
G. miyazakii Anderson, 1964	otter	kidney	North America	
G. malaysiae Miyazaki et Dunn, 1965	rat	stomach	Malaysia, Thailand	
G. vietnamicum Le Van Hoa, 1965	otter	kidney	Vietnam, Thailand	
G. binucleatum Almeyda-Artigas 1991	canine	stomach	Mexico	Yes

(modified from Table I, Daengsvang, 1980)

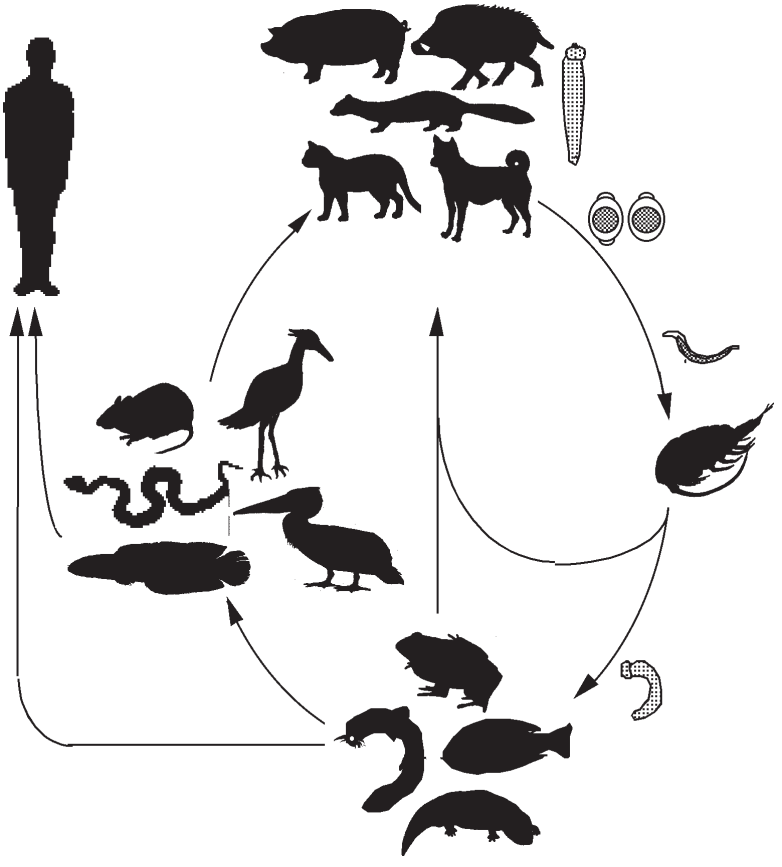

Fig 1- Life cycle of the genus *Gnathostoma*.

addition, an outbreak of gnathostomiasis was found in Ecuador (Ollague *et al*, 1984; Mimori *et al*, 1987) and Mexico (Ogata *et al*, 1998; Diaz Camacho *et al*, 1998; 2003), of which the causative pathogen was identified as *G. binucleatum*. The outbreak in Latin America is considered to be related to the increased consumption of freshwater fish cultivated in dam lakes. Altogether, five *Gnathostoma* spp are now known to cause human disease.

The definitive hosts, the main source of human infection and a rough outline of epidemics of those five *Gnathostoma* spp are summarized in Table 2. In addition to the known endemic areas, recently an outbreak of gnathostomiasis among Korean emigrants in Yangon, Myanmar, was reported as the results of collaboration of Korean and Japanese Embassies in Yangon and the Parasitology institutions (Chai *et al*, 2003). The collaborative study with Danish and Vietnamese scientists revealed that *G. spinigerum* larvae were commonly seen in freshwater fish in Vietnam (De *et al*, 2003), indicating that gnathostomiasis could occur everywhere on the Indochina peninsula. In fact, a case of ocular gnathostomiasis has recently been reported from Vietnam (Xuan *et al*, 2002). Recently we have experienced three cases of gnathostomiasis in Japan who were supposed to be infected while traveling overseas, with one case each in South Africa, Brazil, and Cambodia (Nawa, unpublished data). In Europe and North America, gnathostomiasis cases were occasionally found in emigrants from endemic countries. However, sporadic cases were found among travelers from developed countries who visited endemic areas (Del Giudice *et al*, 2001; Puente *et al*, 2002; Hale *et al*, 2003; Moore *et al*, 2003).

CLINICAL FEATURES OF GNATHOSTOMIASIS

In terms of clinical features, those 5 species will be divided into two groups: a *G. spinigerum* and *G. binucleatum* group, and a *G. hispidum*, *G. nipponicum*, and *G. doloresi* group (Table 3). The former group causes long-lasting recurrent infection in relatively deeper parts of the skin of peripheral sites of the body, whereas the latter group of worms preferentially migrate into the surface skin of the trunks and have a short survival time (<3 months). Of course, such a classification merely shows the general tendency, and the actual clinical manifestation of an individual patient varies from each other.

Cutaneous lesions of gnathostomiasis are somewhat similar to creeping eruption caused by percutaneous infection with dog/cat hookworm larvae. This disease is known among American and European travelers as 'A souvenir of our dream vacation' (Edelglass *et al*, 1982). Such cases have been increasing in Japan among travelers to Southeast Asian resorts (Nakamura-Uchiyama *et al*, 2002). In addition, in Japan, Type X larvae of Spiruroidea are known to cause creeping eruption. The main source of infection is ingesting 'sashimi' of scintillant squid (Okazaki *et al*, 1993; Taniguchi *et al*, 1994).

Apart from cutaneous lesions, occasionally *Gnathostoma* larvae migrate into unexpected sites (Daengsvang, 1980). Migration of larvae into vital organs results in fatal or deleterious illness. CNS involvement was reported in *G. spinigerum* infection

Table 2
Epidemics of gnathostomiasis caused by 5 *Gnathostoma* species.

Species	Definitive host	Source of infection	Epidemics of human infection
G. spinigerum	dogs, cats	snakeheads	1940 till now in Thailand[a] (↓) 1940-1960s in Japan
G. hispidum	pigs, wild pigs	loaches (imported)	1980-1990s Urban areas in Japan
G. doloresi	wild pigs	freshwater fishes	Since 1984 Rural areas in Japan
G. nipponicum	weasels	loaches (domestic)	Since 1986 Sporadic in rural areas in Japan
G. binucleatum	dogs	freshwater fishes	Since 1970 Mexico and Ecuador

[a]gradual decrease with time

Table 3
Clinical features of human gnathostomiasis caused by different species.

Species	Duration	Affected sites	Skin lesion
G. spinigerum *G. binucleatum*	> 1-4 years	peripheral extremities, face, head	erythema > creeping
G. hispidum *G. nipponicum* *G. doloresi*	< 2-3 months	central abdomen, back	creeping > erythema

in Thailand (Vejjajiva, 1978). Cases of ocular involvement have also been reported in *G. spinigerum* infection in Thailand (Daengsvang, 1980; Teekhasaenee *et al*, 1986) and *G. binucleatum* infection in Mexico (Baquera-Heredia *et al*, 2002).

CONCLUSIONS

Gnathostomiasis has been considered a unique fish-borne parasitic zoonosis caused by *G. spinigerum* infection in Asian countries, especially in Thailand and Japan, in relation to their cooking style. However, since the 1970s, heavily endemic areas were found in Latin America, and new causative species have been identified one after another in Japan. Recently, the endemicity of this disease has been all over the Indochina peninsula. Furthermore, sporadic cases have been reported among travelers from northern countries. Gnathostomiasis is, therefore, an important subject for travel medicine. Since detection of *Gnathostoma* larvae from the lesions is extremely difficult, and since the clinical manifestation of gnathostomiasis is somehow similar to other cutaneous larva migrans caused by animal hookworm larvae or by Type X larvae of *Spirurina*, a sensitive and specific immunological test should be developed for differential diagnosis. In terms of clinical manifestations, *Gnathostoma* spp seem to be divided into long-lived and short-lived groups, suggesting different immunogenicity to humans. Molecular taxonomy on the co-evolution of *Gnathostoma* spp and their hosts would elucidate the immunogenicity of each species to humans.

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