GNATHOSTOMIASIS IN SOUTHEAST ASIA

SVASTI DAENGSVANG

Department of Helminthology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand.

Generally speaking gnathostomiasis means the infection or disease in man or animal definitive host being caused by a small roundworm of the genus Gnathostoma. First described was the species, *G. spinigerum* by Richard Owen in 1836 from the stomach tumors of a young tiger that died in the London Zoo. Subsequently there were more species of the genus reported from animals by different authors in various parts of the world. However, it seems that there may be to date 10-12 recognized species of which 5 were reported in Southeast Asia. Of these 5 species, the adult male and female gnathostomes were normally found locating in the stomach wall of the animal definitive hosts causing inflammatory reaction, ulceration and fibrotic formation of the affected parts surrounding the parasites except in case of *G. vietnamicum* infection, the adult worms and larvae were found located in the urinary system of the host, otter (*Lutra elioti* and *Aonyx cinerea.*)

Regarding the human gnathostomiasis although *G. hispidum* was reported twice; one in Japan (Morishita, 1924) and the other case in China (Chen, 1949) otherwise only *G. spinigerum* was frequently reported infecting man in Southeast Asia mostly in Thailand, and few cases were from all other 7 countries (Table 1). The disease seems to be of much concern medically and of a public health problem in Thailand. As a result of the response to the data-report forms sent for tentative clinical survey, a yearly average of about 900 highly suspected human cases during 1961-1963 were diagnosed by doctors of 92 provincial and Bangkok hospitals and one rural health center (Daengsvang *et al.*, 1966). Moreover at least 63 confirmed cases with identification of *G. spinigerum* by the clinicians including some deaths due to the presence of one parasite in the CNS were reported since 1889 to 1979 (Daengsvang, 1980 a).

Identification of Gnathostoma

As previously mentioned, Owen (1836) first described *Gnathostoma* with *G. spinigerum* as its first species. Subsequently Baylis and Lane in 1920 restudied *G. spinigerum* and other species made a key to the subject. Miyazaki (1960) considered also only 7 distinct species of 19 reported up to that year. The author also considered that at present 12 species may be recognized. In species diagnosis of the adults in genus *Gnathostoma*, some specific diagnostic points relating to the worms should be borne in mind as follows:

(i) Size and general body shape.
(ii) Number of rows and the arrangements of cephalic spines or hooklets rows.
(iii) Shape and extent of body cuticular spines.
(iv) For the male worm, the size of caudal pedunculate papillae and Y-shaped spineless area at the posterior end.

Also, after the discovery of the life cycle of *G. spinigerum* and of some others, the size and shape of the body and number and shape of cephalic spines or hooklets of the advanced third-stage larvae as well as the size and morphology of the fertilized eggs were found to be different in certain species. Additionally the definitive hosts and locations of the adult

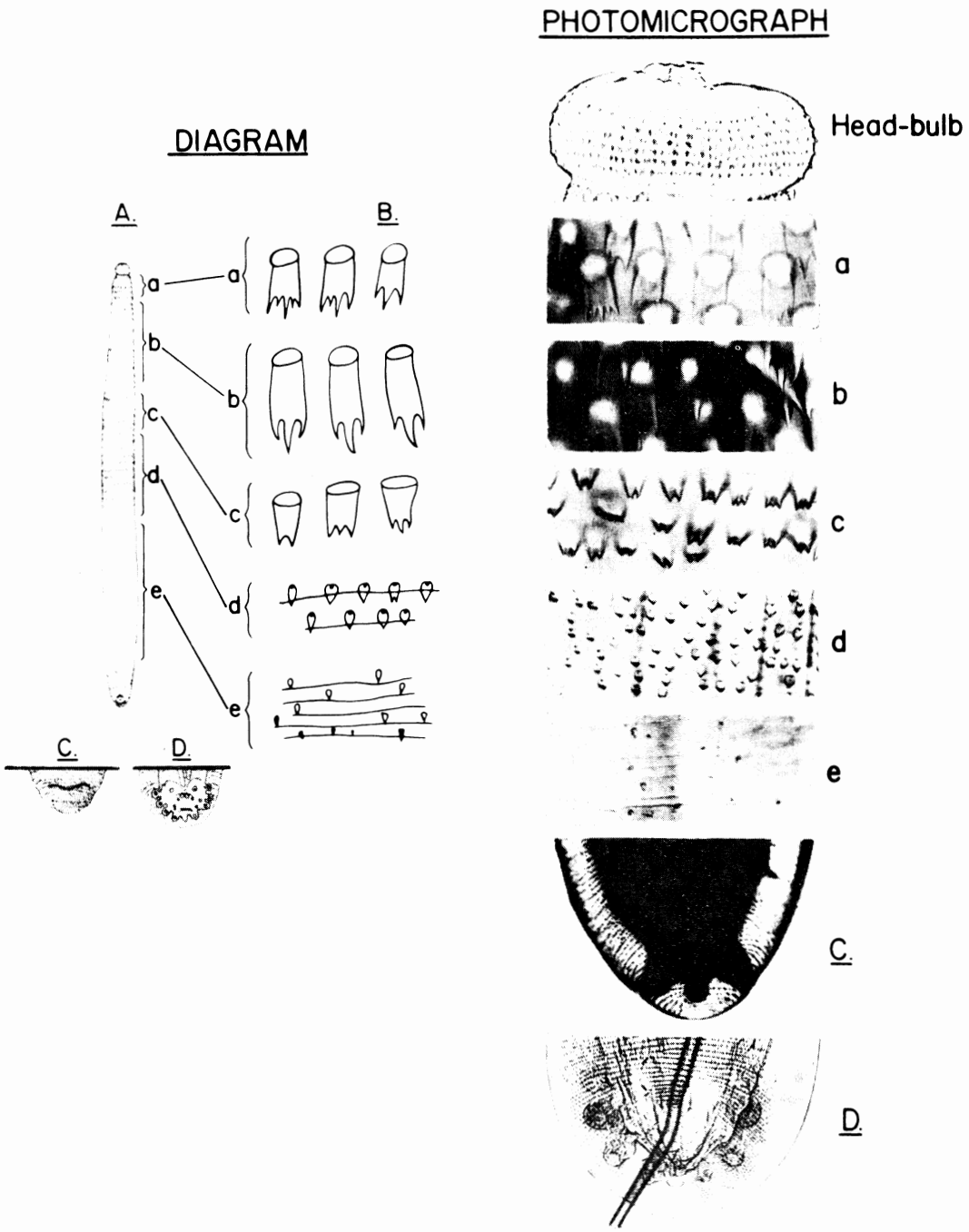


Fig. 1 — Diagram and photomicrograph showing extent and shape of body cuticular spines of adult *G. spinigerum*.
A. Body
B. Cuticular spines
C. Female tail (ventral view) with posteriorly pointed minute spines.
D. Male tail (ventral view) with Y-shaped spineless area around the cloacal aperture and anteriorly pointed minute spines.

worms in them may provide information for consideration in species differentiation. An illustration is shown in Fig. 1, on the shape and extent of body cuticular spines including the tail being considered characteristically among others for adult *G. spinigerum.*

The detailed specific diagnostic characters of 5 species of gnathostomes being reported in Southeast Asia has been presented by Daengsvang (1980a) and by Miyazaki (1960) on the genus *Gnathostoma* and human gnathostomiasis with special reference to Japan. Baylis and Lane (1920) made a revision of nematode Family Gnathostomidae. While Miyazaki and Dunn (1965), reported *Gnathostoma malaysiae* sp. n. (Nematoda : Gnathostomidae) from rats on Tioman Island, Malaysia.

Life cycle

To prevent, control or eradicate any helminthic disease from man or animal, at least one has to have full knowledge on the life cycle of the parasitic species of the worm concerned. In this connection in 1933-1937 Prommas and Daengsvang have shown experimentally for the first time, that to complete the life cycle of *G. spinigerum*, two intermediate hosts were required namely cyclops was the first, and the second was fresh-water fish (*Charias batrachus* Linnaeus or catfish, and *Ophicephalus striatus* Bloch, or snake-headed fish) for the larval development before becoming adult *G. spinigerum* in the stomach wall of the definitive host, cat by ingestion of the larvae in the fish.

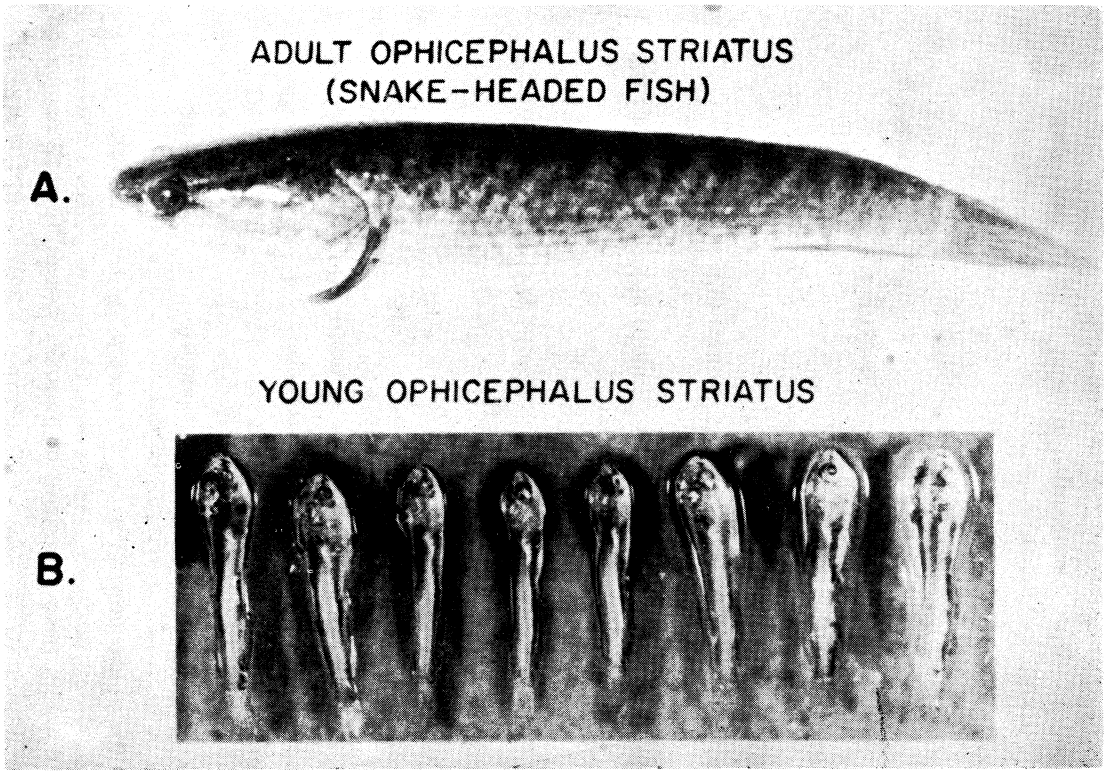


Fig. 2—Close-up photographs of *Ophicephalus striatus* (snake-headed fish), the most significant intermediate host carrying the infection of *G. spinigerum* to man.
A. An adult fish of 600 grams in weight naturally infected in liver and muscles with 153 *G. spinigerum* advanced third-stage larvae.
B. Young fish of Bangkok area, each weighing not more than 5 grams showed the natural infection rate of the worm in livers and muscles 1.2-25.7%.

Table 1

A summary on natural human and animal gnathostomiasis reported in Southeast Asia.

Country \ *Gnathostoma* & Host	*G. spinigerum*			*G. hispidum*		*G. doloresi*		*G. vietnamicum*		*G. malaysiae*	
	Man	Animal		Animal		Animal		Animal		Animal	
		Def.	Intm.	Def.	Intm.	Def.	Intm.	Def.	Intm.	Def.	Intm.
Thailand (1889-1979)	++	Cat (dom. & wild), dog, tiger, leopard	Fish, amphibian, reptile, avian, rodent	Pig (dom.)	-	Pig (dom.)	-	Otter *(Aonyx cinerea)*	-	-	-
Vietnam (1914-1965)	+	Cat (dom. & wild), tiger	Fish	Pig (dom.)	-	Pig (dom.)	-	Otter *(Lutra elioti)*	-	-	-
Philippines (1918-1967)	+	Cat (dom.) dog	Fish	Pig (dom.)	-	Pig (dom.)	-	-	-	-	-
Malaysia (1933-1976)	+	Cat (dom.), civet cat, tiger, leopard	-	-	-	Pig (dom.)	-	-	-	Rattus	-
Burma (1957-1968)	+	Cat (dom.)	-	-	-	Pig (dom.)	-	-	-	-	-
Cambodia (1963-1976)	+	-	-	Pig (dom.)	-	-	-	-	-	-	-
Laos (1975)	+	-	-	-	-	-	-	-	-	-	-
Indonesia (1949)	+	-	-	-	-	-	-	-	-	-	-

NOTE. ++ Many Cases, + 1-3 Cases; Def. = Definitive. Intm. = Intermediate.

The total time required for the complete life cycle; that is the development of the adult worms in the stomach wall of the cats was about 7 months. Sooksri (1967) identified 4 species of cyclops namely *Mesocyclops leuckarti*, *Eucyclops agilis*, *Cyclops varicans* and *Thermocyclops* sp. acting experimentally as the first intermediate host. Daengsvang (1980 a) summarised 44 species of vertebrate being naturally infected with *G. spinigerum* advanced third-stage larvae by many authors in Thailand of which the fresh-water fish (*Ophicephalus striatus*) is considered to be the most significant intermediate host carrying the infection of the worm to man (Fig. 2). In the Philippines, (Africa *et al.*, 1936 a) reported natural infection with presumably *G. spinigerum* larvae in 2 species of fresh-water fish and one species of aquatic snake. To date after a summary of the literature, the definitive hosts of this worm recorded in Thailand and 4 other countries in Southeast Asia were, domestic and some wild cats, dogs, tigers and leopards (Table 1). Diagram of the life cycle of *G. spinigerum* is shown in Fig. 3.

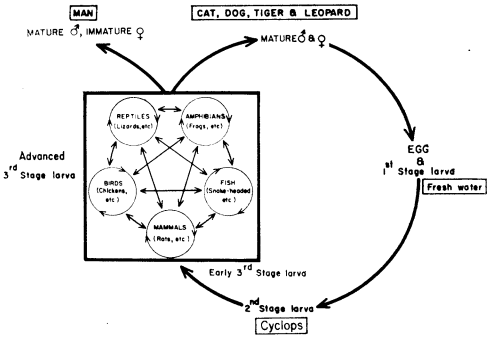


Fig. 3—Life cycle of *Gnathostoma spinigerum* in Thailand.

G. hispidum Fedchenko 1872: The adult worms of *G. hispidum* were first described by Fedchenko 1872 from the gastric wall of wild and domestic pigs of Turkestan and Hungary. In the stomach wall of Southeast Asian pigs, the adult of this species was reported from Vietnam, Philippines, Cambodia and Thailand. Barus and Moravec (1969) in Czechoslovakia reported a fragment of the male worm in the stomach cavity of the cadaver of an otter (*Aonyx cinerea*) imported from Malyasia, this last case may need further clarification.

Golovin (1956) has first experimentally shown that the infection of the definitive host, pig could be possible by either (1), drinking water containing infected cyclops or (2), eating the larva-infected hosts (fish, amphibians,reptiles). In Thailand, Dissamarn *et al.*, (1966) experimentally discovered that *Mesocyclops leuckarti* was the first intermediate host and 7 months later the adult *G. hispidum* could develop in the stomach wall of the domestic pig after being fed with the infected cyclops. Daengsvang (1972) reported that *G. hispidum* could develop in the stomach wall of the experimental pigs 5-7 months after being directly fed with the infected cyclops or about 8 months after being fed with the advanced third-stage larvae obtained from the experimentally infected fresh-water fish, amphibians and rodents, thus confirming findings of Golovin (1956) and Dissamarn *et al.*, (1966). The life cycle of this gnathostome is shown in diagram (Fig. 4).

G. doloresi Tubangui, 1925 life cycle needs two intermediate hosts as follows: The adult

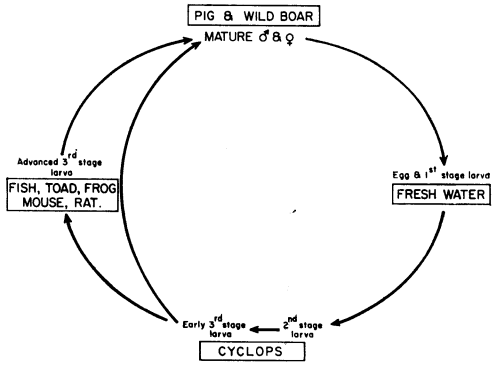


Fig. 4—Life cycle of *Gnathostoma hispidum*.

female worms were first described by Tubangui in 1925 from the stomach wall of a pig in Luzon, Philippines and later Maplestone (1930) described the male worms from the stomach wall of pigs in India. Sandosham (1953) reported a male and a female *G. doloresi* from the liver of a pig in Malaysia. In Vietnam, Le-Van-Hoa *et al.*, (1965) reported from the pigs. In Thailand, Dissamarn *et al.*, (1966), Daengsvang *et al.*, (1968) reported the adult male and female worms from the stomach of domestic pigs. The larval development needs cyclops as the first intermediate host for developing to the early third-stage larvae, about 9-10 days after being fed with the first stage or newly hatched larvae from the eggs. Further development of these larvae in cyclops to become the advanced third stage was found to be a few days after being ingested by the second intermediate host namely toad, frog, white mice and domestic rat. The adult worms could develop in the stomach wall of the pig after being fed with the advanced third-stage larvae perhaps about 10 months.

In Japan, Ishii (1956), Miyazaki (1960), Miyazaki and Kawashima (1962) and Tada *et al.*,(1969) reported salamander of the genus Hynobius (*H. naevius*, *H. stejnegeri*) and snake infected naturally with the encysted gnathostome larvae. The larvae obtained from the salamander became adult *G. doloresi* in the gastric wall of a wild boar and a pig in 5 months and 3 months respectively after the feeding experiment. The life cycle of *G. doloresi* is shown in Fig. 5.

G. vietnamicum Le-Van-Hoa 1965 was first found infecting the kidney of otters (*Lutra elioti* Hogson) and described by Le-Van-Hoa (1965) from Vietnam, and the urinary system including kidney, ureter and urinary bladder of otters (*Aonyx cinerea* Illiger) from Thailand (Daengsvang *et al.*, 1969 a; Daengsvang, 1973). A preliminary experimental study on its life cycle was made,

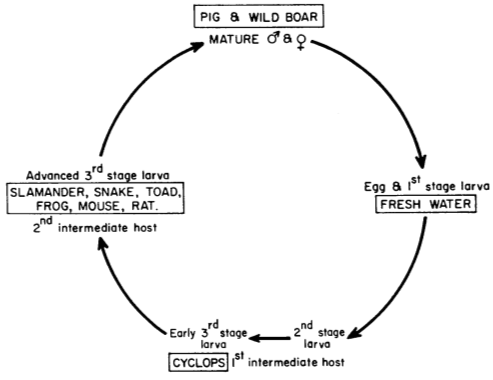


Fig. 5 Life cycle of *Gnathostoma dolresi*.

although incomplete, showed that the newly laid one-or two-cell fertilized eggs needed 15-17 days in water at room temperature of 29°-30°C to become newly hatched larvae and the larvae after being ingested by *Mesocyclops leuckarti* Claus, for about 15 days become early third stage in the body cavity of the crustacean. One of the two small fighting fish (*Trichopsis vittatus*) was found to be infected with one living undeveloped larva in its stomach wall 21 days after being fed with a total of 16 fully developed larvae from cyclops (Daengsvang, 1973).

A diagram of the incomplete information on life cycle of this worm is shown in Fig. 6.

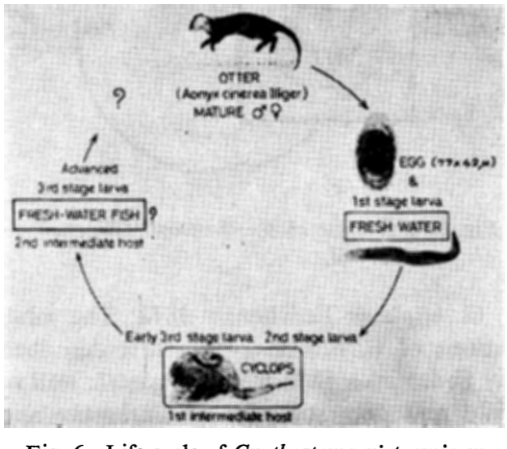


Fig. 6 Life cycle of *Gnathostoma vietnamicum*.

Methods of Transmission

To date experimentally 3 methods of transmission of gnathostomes are proven possible.

Ingestion: This is the first proven method shown by the experiment on *G. spinigerum* infection in cat by feeding on the infected flesh of the fresh-water fish; *Ophicephalus striatus* (snake-headed fish), *Clarias batrachus* (cat-fish) (Prommas and Daengsvang, 1937). Golovin (1956) also successfully showed by the experiment on pigs that *G. hispidum* transmission could be possible by either ingestion of the cyclops or vertebrates (fish, amphibian, reptiles) infected with the larval stage. The same was shown in G. *doloresi* that the definitive host, pig become infected with the adult *G. doloresi* by ingesting the advanced third-stage larvae harbouring in the muscle of the salamander (Miyazaki, 1960). Then it is assumable that oral transmission can be expected in all species of gnathostomes.

Skin penetration: *G. spinigerum* advanced third-stage larvae through skin penetration was experimentally proved in cat and dog; also the life cycle of the parasite could be completely shown by this method of transmission. The period required for the development into adult worms after skin penetration of the larvae in few cases is shorter than after oral infection (Daengsvang *et al.*, 1970 a, b). In man the migration of the larval stage after skin penetration might be similar to that found in the definitive host. This method has not yet been investigated with other species of gnathostomes.

Prenatal transmission: Of the 152 offsprings born from 22 experimentally infected pregnant white mice, two had one unencysted *G. spinigerum* third-stage larva each; one larva was found in the liver and the other in the costal muscles when necropsies were done soon after their births. Two human gnathostomiasis cases discovered in babies have been suggested that the infection may occur prenatally (Daengsvang, 1968). The method has not been known with other gnathostome infections.

Symptoms and signs

The infection or disease caused by adult or migrating stages of *G. spinigerum* normally produces symptoms and signs in the infected hosts due to mostly gnathostome toxin consisting of many factors, namely substance resembling acetylcholine, spreading factor containing hyaluronidase, proteolytic enzyme and hemolytic substance (Miyazaki, 1960). The mechanical action done by the migrating worm and the reaction of the affected part of host play also some part in giving rise to symptoms and signs.

In this regard it may be assumed that a similar toxin would be produced by other species of *Gnathostoma* and as a result of the infection some similar signs and symptoms could be expected in the infected host due to the action of the parasite and its toxin as well as the reaction of the host.

In general, gnathostomiasis may be known in two types of host namely:

(1) Human gnathostomiasis.

(2) Animal gnathostomiasis.

Almost all human gnathostomiasis cases were caused by *G. spinigerum*, however two cases of *G. hispidum* infection were reported; one in Japan showing skin infection (Morishita, 1924) and the other of ocular disease (Chen, 1949). Subsequently, Miyazaki (1960) was sceptical about the identification of the two cases.

Regarding the disease in man many clinicians and parasitologist often classify the cases into two groups; gnathostomiasis externa and gnathostomiasis interna.

The external or cutaneous gnathostomiasis or gnathostomiasis externa shows symptoms and signs on the skin or mucous membrane

as follows: (i) Intermittent migratory swelling of various circumscribed sizes at places of which each normally shows no pitting on pressure lasting for about one or two weeks (Fig. 7A, B, C) except in one instance a hard non-tender and movable subcutaneous tumor about 3 × 2 cm found in occipital region was almost symptomless for two months (Nitidandhaprabhas *et al.*, 1978), and rare cases of creeping eruptions were recognized; (ii) signs and symptoms of inflammatory reaction over the affected parts; (iii) itching or irritation and pain accompanying the swelling area. In some cases the swellings may show either itching without pain or vice versa. In rare occasions, the swellings show neither itching nor pain; (iv) slight moving pain with itching sensation or irritation without swelling was recognized subcutaneously in one case (Nitidandhprabhas *et al.*, 1975), (v) General health condition is usually normal.

Gnathostomiasis interna or internal or visceral gnathostomiasis has been reported in many visceral organs including respiratory system, gastrointestinal tract, genito-urinary tract, eye-ball, etc., a result of the damage done by the worm and host tissue reactions according to the affected parts; acute and chronic inflammation accompanying with hemorrhages, necrotic change, swelling, fibrous formation or tumor with or without pressure symptoms, irritation and tenderness or pain were reported. Symptoms complex of severe agonizing pain over the trunk and lower extremities followed by paralysis, unconciousness due to much damage of CNS by one *G. spinigerum* causing eosinophilic myeloencephalitis and death have been recorded (Fig. 7 D).

To date *G. spinigerum* is found causing visceral gnathostomiasis with the above-mentioned symptoms and signs, or human death in Southeast Asia except one case of ocular gnathostomiasis by *G. hispidum* (Chen, 1949).

Diagnosis

Logically the diagnosis of human gnathostomiasis should be confirmed by identification of the worm. However, the following clinical and laboratory findings of the cases without the parasite may be useful for the diagnosis of the infection:

(1) Clinical symptoms and signs for external and visceral gnathostomiasis,

(2) Previous history of exposure to the infection by eating raw or half-cooked infected flesh of fresh-water fish, chicken etc. Also long continuing skin contact with the infected flesh may give rise to the infection through the skin.

(3) Intra-cutaneous or skin test positive by using gnathostome antigen (Miyazaki, 1960) may be helpful for consideration with other findings of the suspected case.

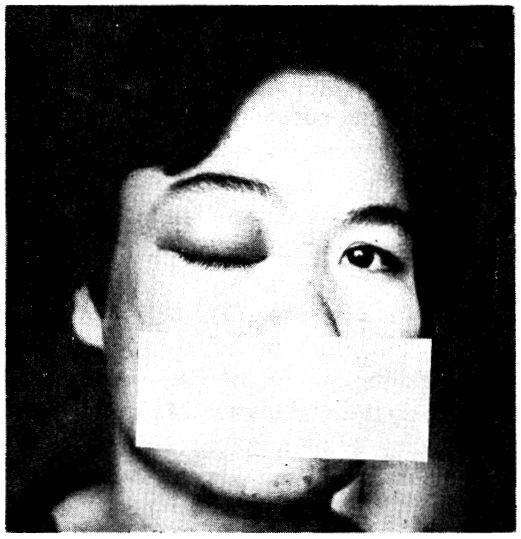
(4) With few exceptions, otherwise the peripheral blood picture usually show in most cases moderate degree of eosinophilia with variations of about 10-96%, and slight or moderate leucocytosis in some cases.

Regarding animal gnathostomiasis, information may be briefly presented as follows:

G. spinigerum infection: Adult *G. spinigerum* infections have been reported in the stomach wall, rarely other parts of the gastro-intestinal tract, of carnivorous animals acting as the definitive hosts of the worm. These animals are important reservoirs or definitive hosts for spreading the infection among themselves as well as spreading to man now being considered as the accidental host. The animals, after being moderately or heavily infected, may die either of perforation of the infected stomachs and peritonitis or gastritis and ulceration followed by lack of food. The worms usually cause inflammation, hemorrhage, ulceration, fibrous formation and tumors of the stomach wall in which they

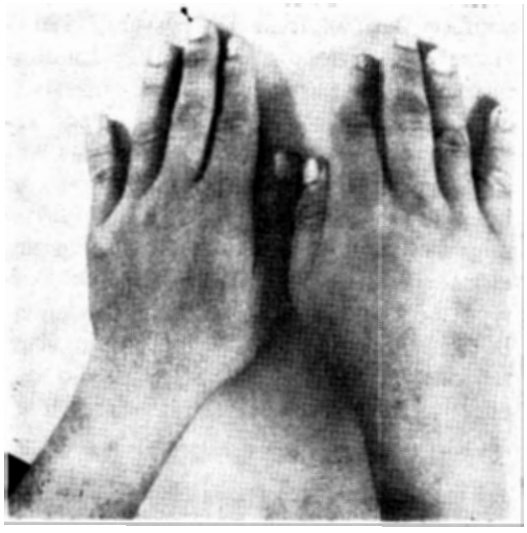
A

Swelling of the right cheek.



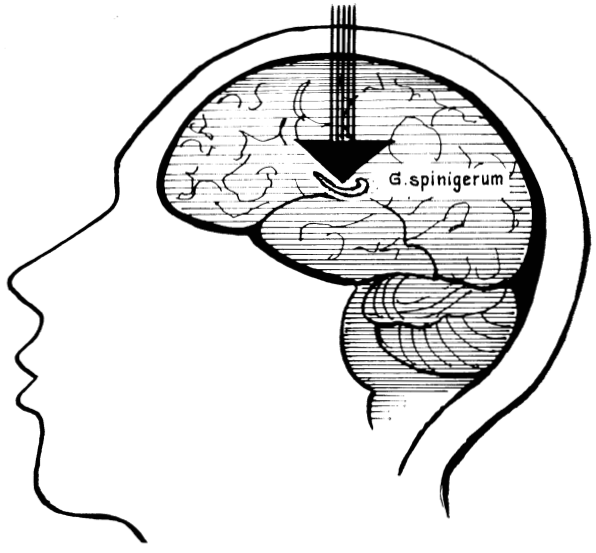
B

Swelling of the right eyelid.



C

Swelling of the right hand.



D

A diagram of the brain with presence of the worm in the cerebrum.

Fig. 7 — Photographs and a diagram showing cases of human gnathostomiasis.

are found living in the small tracts with small openings into the stomach cavity of the host. Characteristic eggs can be microscopically discovered in the exudates obtained from the tracts, stomach contents, and the stool of the infected animals. The animals if still alive showed spontaneous cure of the infection in about few months (Daengsvang *et al.*, 1969 b).

G. hispidum Fedchenko, 1872 and *G. doloresi* Tubanqui, 1925, may be called pig gnathostomes because up to now they are found infecting only the stomach wall of pig and wild boar causing small localized inflammatory areas, hemorrhage, ulceration and small fibrotic thickening of the infected inner wall of the stomach, never produced well-developed tumors as found in the stomach wall of a cat infected with *G. spinigerum*. They may cause malnutrition in moderately or heavily infected animals. However, Maplestone (1930) considered that even though only one or two adult worms *G. doloresi* were found present in the stomach wall in pigs in Bengal, India, it must be very serious, even if not at the time fatal, since the worms caused extensive damage to the stomach wall in which they burrowed deeply.

G. vietnamicum Le-Van-Hoa, 1965 adult worms and the larval stage were found located in the kidneys of otters (*Lutra elioti* Hogson). In Thailand, Daengsvang *et al.*, (1968, 1969 a) and Daengsvang (1973) reported the adults and presumably larvae, in the urinary system; kidneys, ureters and urinary bladder of otters (*Aonyx cinerea* Illiger) (about 43.0 %). The infected areas showed ulcerative and fibrotic changes with or without association of calcification. In one case a small smooth hard stone was seen embedded in the infected kidney. If few gnathostomes of this species were found in both kidneys it may the fatal to the infected otters due to the damage done by the worms at the infected areas.

G. malaysiae Miyazaki and Dunn. 1965 was first found and reported from the stomach wall of rats; *Rattus surifer* and *Rattus rattus tiomanicus* trapped in Tioman Island, Malaysia. The worms according to the authors, were parasitic in separate out-pouching of the stomach wall (Miyazaki and Dunn, 1965). To date the study on the life cycle of this worm has not been determined.

Treatment and Prevention

None of may anthelmintic drugs on tissue infected helminths has been known to have therapeutic effects by screening test done on mice experimentally infected with *G. spinigerum* advanced third-stage larvae namely; Bithionol (bitin), Thiabendazole, Niridazole (ambilhar), Banocide (hetrazan), Hetol, Fouadin, Flagyl, Dehydroemetine, Metrifonate, Astiben, Lucanthone, Hycanthone, Lugol's solution, Trodax, Jonit (Daengsvang, 1980 a). However, Ancylol disophenol, (2, 6-diiodo-4-nitro-phenol) parenteral 4.5% effectively eliminated adult *G. spinigerum* from the gastrointestinal tract of 7 infected cats with a single dose of 0.1 ml per pound body weight, but the dosage showed no effect on the migrating stage in the cats'tissue (Daengsvang *et al.*, 1971). Later, Daengsvang (1980 b) reported that 12 doses of 0.05 ml per pound body weight of the Ancylol given subcutaneously at 10-day intervals showed a very effective result on migrating stage of *G. spinigerum* in 2 cats.

This Ancylol is very toxic to man, therefore at present it can not be recommended for human use.

X-ray irradiation had an anti-inflammatory action but no anthelmintic action could be expected (Miyazaki, 1966). The treatment now is surgical removal of the worm if the parasite can be precisely located and that surgery can be safely done especially in some external human gnathostomiasis cases, ocular gnath-

ostomiasis, interaabdominal infection etc. (Daengsvang, 1980a).

A case of gnathostomiasis (Japanese patient) in Yokohama was treated with thiabendazole with good results or cure in 1977 (Oshima and Fujita, 1977). The report seems to be challenging for more investigations on the issue.

Many human gnathostomiasis cases may need in a short period, effective chemotherapeutic treatment before the worm could greatly damage the affected organs and kill the patient especially those involving the CNS. It is justifiable that united effort should be made to find the solution for the problem in man, because human deaths have been reported caused by only one *G. spinigerum* (Chitanondh and Rosen, 1967; Punyagupta *et al.*, 1968; Boongird *et al.*, 1977).

As regard to the prevention of human and animal gnathostomiasis in a community, now the effective chemotherapy of Ancylol disophenol is known for eliminating the causative worm from the gastrointestinal tract and tissue of the definitive host, cat, but the detailed application of this knowledge for the control of the disease remains a problem.

At present, the most important knowledge of individual preventive measures against the human infection is in principal, sufficiently known especially, not to eat raw or half-cooked animal flesh suspected to be the source of the infection, now known to be 44 species of vertebrate (Daengsvang, 1980 a) unless thoroughly cooked etc., those persons involved in the long handling of animal flesh for business or family use, bare-handed, might be vulnerable to the skin penetration by the larvae, it is then suggested that frequent cleaning of hands with water and soap should be practiced or wearing thick rubber gloves while preparing the flesh of the animal, and to drink properly treated water in endemic areas of the infection because the untreated water especially from the shallow wells or surface ground water collections might be contaminated with the living infective larvae after being separated from the decomposed flesh of dead infected intermediate or paratenic hosts.

SUMMARY

Five species of *Gnathostoma* are at present reported from Southeast Asia with specific diagnostic characteristic of each. Also important references relating to the specific characters of the species concerned were mentioned, and the known experimental life cycles of three species namely *G. spinigerum*, *G. hispidum*, and *G. doloresi* found in the region were compared. The incomplete experimental study on the life cycle of *G. vietnamicum* is presented but the investigation on the life cycle of *G. malaysiae* is not yet initiated. Methods of transmission, symptoms and signs, the diagnosis and treatment of animal and human gnathostomiasis were also summarized.

Effective therapeutic value of many anthelmintic drugs has not been satisfactory, by screening test on white mice previously infected in the tissue with *G. spinigerum* larvae. However, successful result of treatment was reported on one Japanese gnathostomiasis patient with thiabendazole.

In the treatment of animal gnathostomiasis, Ancylol disophenol seems to be the effective drug for eliminating adult and migrating stage in the experimentally infected cats. Brief preventive measures against human gnathostomiasis was mentioned.

ACKNOWLEDGEMENTS

The author wishes to express appreciation to publishers of the Southeast Asian Medical Information Center (SEAMIC) Tokyo, Japan

and Annals of Tropical Medicine and Parasitology, Liverpool, England for their permissions to publish figures and information obtained from a monograph on the genus Gnathostoma and gnathostomiasis in Thailand and from some publications of the Annals respectively.

REFERENCES

AFRICA, C.M., REFUERZO, P.G. and GARCIA. E.Y., (1836). Observation on the life cycle of *Gnathostoma spinigerum*. *Phil. J. Sci.*, *59* : 513.

BARUS, V. and MORAVEC, F., (1969). There interesting nematodes from *Aonyx cinerea* (Carnivora) from Malaya. *Folia Parasit.*, *16* : 235.

BAYLIS, H.A. and LANE, C., (1920). A revision of nematode Family Gnathostomidae. *Proc. Zool. Soc. London*, p. 245.

BOONGIRD, P., PHANPRADIT, P., SIRIDEJ, N., CHIRACHARIYAVEJ, T., CHUAHIRUN, S. and VEJJAJIVA, A., (1977). Neurological manifestations of gnathostomiasis *J. Neurol. Sci.*, *31* : 279.

CHEN, H.T., (1949). A human ocular infection by *Gnathostoma* in China. *J. Parasit.*, *35* : 431.

CHITANONDH, H., and ROSEN, L., (1967). Fatal eosinophilic encephalomyelitis caused by the nematode *Gnathostoma spinigerum*. *Amer. J. Trop. Med. Hyg.*, *16* : 638.

DAENGSVANG. S., (1968). Further observations on the experimental transmission of *Gnathostoma spinigerum*. *Ann. Trop. Med. Parasit.*, *62* : 88.

DAENGSVANG, S., (1972). An experimental study on the life cycle of *Gnathostoma hispidum* Fedchenko, 1872 in Thailand with special reference to the incidence and some significant morphological characters of the adult and larval stages. *Southeast Asian J. Trop. Med. Pub. Hlth.*, *3* : 376.

DAENGSVANG, S., (1973). First report on *Gnathostoma vietnamicum* Le-Van-Hoa, 1965 from uninary system of otters (*Aonyx cinerea* Illiger) in Thailand. *Southeast Asian J. Trop. Med. Pub. Hlth.*, *4* : 63.

DAENGSVANG, S., (1980 a). A monograph on the genus Gnathostoma and gnathostomiasis in Thailand. SEAMIC Southeast Asian Medical Information Center. Tokyo, Japan.

DAENGSVANG, S., (1980b). Chemotherapy of feline *Gnathostoma spinigerum* migrating stage with multiple subcutaneous doses of Ancylol. *Southeast Asian J. Trop. Med. Pub. Hlth.*, *11* : 359.

DAENGSVANG, S., THIENPRASITH, P., CHOMCHERNGPAT, P. and PHRUKOUDOM, B., (1966). Gnathostomiasis in Thailand. *Ann. Prog. Rept. U.S. Army Med. Comp. SEATO.*, p. 106.

DAENGSVANG, S., PECHARANOND, K., SERMSWATSRI, B., YOUNGYI, P. and GUNAME, D., (1968). Studies on gnathostomiasis in Thailand. *Ann. Prog. Rept. SEATO Med. Res. Lab. SEATO Clin. Res. Cent.*, p. 196.

DAENGSVANG, S., SERMSWATSRI, B., YOUNGYI, P. and GUNAME, D., (1969 a). Studies on gnathostomiasis in Thailand. *Ann. Prog. Rept: SEATO Med. Res. Lab. SEATO Clin. Res. Cent.*, p. 133.

DAENGSVANG, S., SERMSWATSRI, B. and YOUNGYI, P., (1969 b). Spontaneous cure of the natural and induced *Gnathostoma spinigerum* infection in cats. *Ann. Trop. Med. Parasit.*, *63* : 489.

DAENGSVANG, S., SERMSWATSRI, B., YOUNGYI, P. and GUNAME, D., (1970 a). Development of adult *Gnathostoma spinigerum* in the definitive host (cat, dog) by skin penetration of the advanced third-stage

larvae. *Southeast Asian J. Trop. Med. Pub. Hlth., 1* : 187.

DAENGSVANG, S., SERMSWATSRI, B., YOUNGYI, P. and GUNAME, D., (1970 b). Penetration of the skin by *Gnathostoma spinigerum* larvae. *Ann. Trop. Med. Parasit., 64* : 399.

DAENGSVANG, S., SERMSWATSRI, B., YOUNGYI, P. and GUNAME, D., (1971). A preliminary study on chemotherapy of *Gnathostoma spinigerum* infections in cats with Ancylol disophenol (2, 6-diiodo-4-nitrophenol). *Southeast Asian J. Trop. Med. Pub. Hlth., 2* : 359.

DISSAMARN, R., THIRAPAT, K., ARANYAKANADA, P., and CHAI-ANAN, P., (1966). Studies on morphology and life history of *G. doloresi* and *G. hispidum* inThailand. *J. T. V. M.A., 17* : 1.

FEDCHENKO, A.P., (1872). Zoologitjeskija Samjetki. *Trans. Soc. Nat. Moscow*, X. pp. 100-111, pls xivxv. (Russian), quoted from Baylis and Lane 1920. A revision of the nematode family Gnathostomidae. *Proc. Zool. Soc. London*, p. 245.

GOLOVIN, O.V., (1956). Biology of the nematode *Gnathostoma hispidum. Doklady Akad. Nauk. U.S.S.R.*, 111 (1) 242 (in Russian).

ISHII, Y., (1956). Studies on the life history of *Gnathostoma doloresi* Tubangui, 1925 in Japan. *Fukuoka Acta Med., 47* : 1474, (in Jap. with Engl. abstr.).

LE-VAN-HOA, (1965). Etude d'un nouveau gnathostome *G. vietnamicum* n. sp. chez *Lutra elioti* du Vietnam. *Bull. Soc. Path. Exot., 58* : 228. (in Fr. with Engl. summary).

LE-VAN-HOA, NGUYEN-AI and TA-VAN-LUYEN, (1965). Gnathostomes et gnathostomose humaine au Vietnam. *Bull. Soc. Path. Exot., 58* : 236. (in Fr. with Engl. summary).

MAPLESTONE, P.A., (1930). Nematode parasites of pigs in Bengal. *Records Indian Museum*, 32 (part 2) 77.

MIYAZAKI, I., (1960). On the genus *Gnathostoma* and human gnathostomiasis, with special reference to Japan. *Exp. Parasit., 9* : 338.

MIYAZAKI, I., (1966). Gnathostoma and gnathostomiasis in Japan. *Prog. Med. Parasit. Japan, 3* : 531.

MIYAZAKI, I. and KAWASHIMA, K., (1962). On the larval *Gnathostoma doloresi* Tubangui found in a snake from Ishikagi-jima, the Ryukyu Islands (Nematoda : Gnathostomidae). *Kyushu J. Med. Sci., 13* : 165.

MIYAZAKI, I. and DUNN, F.L., (1965). *Gnathostoma malaysiae* sp. n. from rats on Tioman Island, Malaysia (Nematoda: Gnathostomidae) *J. Parasit., 51* : 382.

MORISHITA, K.O.R., (1924). A pig nematode *Gnathostoma hispidum* Fedchenko, as a human parasite. *Ann. Trop. Med. Parasit., 18* : 23.

NITIDANDHPRABHAS, P., HANCHANSIN, S. and VONGSLOESVIDHYA, Y., (1975). A case of expectoration of *Gnathostoma spinigerum* in Thailand. *Amer. J. Trop. Med. Hyg., 24* : 547.

NITIDANDHPRABHAS, P., HARNSOMBURANA, K., SURASVADI, C. and MAHUNEE, W., (1978). A case of occipital gnathostomiasis in Thailand. *Amer. J. Trop. Med. Hyg., 27* : 206.

OSHIMA, T. and FUJITA, K., (1977). A case of gnathostomiasis in Yokohama and its treatment by thiabendazole. Proc. Reg. Meet. Jap. Soc. Parasit. (No. 1) of 37th East Japan Regional Meeting of Parasitology, Tokyo, *Jap. J. Parasit., 26* : 7. (Suppl.).

OWEN, R., (1836). Anatomical descriptions of two species of Entozoa from the stomach of a tiger (*Felis tigris* Linn.) one of which forms a new genus of Nematoidea,

Gnathostoma. *Proc. Zool. Soc., London, 47* : 123.

PROMMAS, C. and DAENGSVANG, S., (1933). Preliminary report of a study on the life cycle of *Gnathostoma spinigerum. J. Parasit., 19* : 287.

PROMMAS, C. and DAENGSVANG, S., (1936). Further report of a study on the life cycle of *Gnathostoma spinigerum. J. Parasit., 22* : 180.

PROMMAS, C. and DAENGSVANG, S., (1937). Feeding experiments on cats with *Gnathostomas spinigerum* larvae obtained from the second intermediate host. *J. Parasit., 23* : 115.

PUNYAGUPTA, S., JUTTIJUDATA, P., BUNNAG. T. and COMER, D.S., (1968). Two fatal cases of eosinophilic myeloencephalitis a newly recognized disease caused by *Gnathostoma spinigerum. Trans. Roy. Soc. Trop. Med. Hyg., 62* : 801.

SANDOSHAM, A.A., (1953). Malaysian parasites. XV, Seven new worms from miscellaneous hosts. *Stud. Inst. Med. Res. Malaya, 26* : 212.

SOOKSRI, V., (1967). Studies on different species of cyclops in Bangkok and neighbouring areas with reference to those acting as first intermediate host of *Gnathostoma spinigerum.* A thesis submitted to the Faculty of Graduate Studies, University of Medical Sciences (now Mahidol University).

TADA, I., SATO, A. and NAGANO, K., (1969). On the larval *Gnathostoma doloresi* found in snakes, *Trimeresurus flavoviridis, flavoviridis* from Amamioshima Is., Kagoshima Japan. *Jap. J. Parasit., 18* : 289.

TUBANGUI, M.A., (1925). Metazoan parasites of Philippine domesticated animals. *Phil. J. Sci., 28* : 11.