Title: Eosinophilic Meningoencephalitis in Thailand

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OBJECTIVE

Continuation of epidemiologic, clinical, neuropathologic, and experimental studies on eosinophilic meningoencephalitis.

DESCRIPTION

A research station has been established in Saraburi province. Suspected cases attending the outpatient clinic and those admitted to the Saraburi Provincial Hospital were studied. Clinical and epidemiologic studies in Bangkok were continued. Efforts were made to obtain autopsies in all fatal cases at these hospitals and also at Udorn Provincial Hospital. Experimental studies are designed to explore the mechanism of central nervous system involvement of Gnathostoma.

PROGRESS

1. Epidemiologic During the past year, 73 new cases of eosinophilic meningitis were studied, making a total of 719 cases since the beginning of the study. Of these patients, 534 are typical cases and 185 belong to myeloencephalitis type. The ratios of the typical form to the myeloencephalitis form are 6:1 in Bangkok, 1:1.6 in Ubon, 26:1 in Udorn, 24:1 in Korat, 1:2 in Lopburi, 1:1 in Saraburi, and 6:1 in Pra Buddhabat. (Table 1)

Six groups of patients were studied. The incubation period varied from 3 to 18 days with an average of 8 days. Pila snails collected from some of thess areas were examined for infective larvae of A. cantonensis. Only 29 out of 134 snails were positive with 1 to 90 with the average of 17 larvae per positive snail.

Because 97 out of 161 cases of eosinophilic myeloencephalitis studied during the previous years showed bloody or xanthochromic spinal fluid, cases of cerebral vascular hemorrhage admitted to these three hospitals were analysed. (Table 2) Cerebral vascular bleeding is a significant disease among the Thai inspite of the fact that vascular abnormalities such as aneurysm are not common compared to western standards. It is concluded from this study that Gnathostoma spinigerum is responsible as a significant cause of intracranial hemorrhage in Thai people particularly in younger age group of 21—40 years (Fig. 1). The prevalence of the condition varies according to the localities (Table 2) and seasons (Fig. 2).

2. Clinical Study

A. Typical Eosinophilic Meningitis

Fifty of the 73 cases were examples of the typical form of eosinophilic meningitis. The clinical manifestations in these cases are not different from previous reports. There has been no mortality.

For the first time in Thailand, Angiostrongylus cantonensis larvae were recovered from the cerebrospinal fluid of a typical case admitted to Pra Buddhabat Hospital. The definite date of infection was known. Living A. cantonensis larvae were recovered on 3 occasions; two larvae on the 8th day, nine larvae on the 11th day, and one larva on the 18th day after infection. (Fig. 3,4) These findings offer the first opportunity to study the growth and development of A. cantonensis in man. It is obvious from our comparative study of man and rat that man is the better host for A. cantonensis. (Table 3, 4)

Clumps of white cells firmly attached around the living worm's body were noted, particularly on the 11th and 18th day after infection. This may be one explanation why larvae are most difficult to recover during the spinal tapping.

B. Myeloencephalitis type

During this period, 23 myeloencephalitis cases were studied. They presented in the form of paraplegia in 6 cases, hemiplegia in 4, monoplegia in one, coma in 4, root pain in 6 and severe headache in 2. Death occurred in one patient but no permission for an autopsy was granted. In these 23 cases, 16 patients showed evidence of intracranial bleeding.

3. Pathological Studies

During the period cross sections of A. cantonensis were seen in a brain specimen of a patient who died at Chulalongkorn Hospital in 1966. This is the fourth proven case. The brain was initially studied by Dr. S.W. Nye and associates. The cross section of the worm measured 300 μ which was the largest A. cantonensis recovered in human brains. The brain tissues were then dissected and 3 pieces of a single worm were found (Fig. 5). The tail end of the worm could not be recovered to distinguish its sex. The incomplete worm measured more than 1.8 cm. in length and 0.35 – 0.41 mm. in width. This is the size of an adult A. cantonensis. In addition the pigmented intestine was noted. This finding supports the impression that man is a suitable host for development of A. cantonensis.

Small areas of gross hemorrhage were noted in the coronal brain sections. This unusual finding in A. cantonensis infection may be explained on the basis of the unusually large size of the worm. These hemorrhagic lesions can be distinguished from those produced by Gnathostoma by the smaller extent and fewer sites of hemorrhages. (Fig. 6) The lesions caused by these 2 parasites can be differentiated as shown in Table 5.

This year there has been no post mortem in the studied cases; however, Dr. Comer performed an autopsy in a patient who died at Udorn Hospital. Cross sections of A. cantonensis larvae were seen. This is the fifth proven post mortem case of A. cantonensis in Thailand.

4. Experimental Study

We have just begun to investigate the mode of central nervous system invasion by Gnathostoma spinigerum. We are able to demonstrate in one experiment that by oral infection in mice, Gnathostoma can readily enter the C.N.S. More experimental work should be done to clarify this point.

Summary At the end of the fourth year 534 cases of typical eosinophilic meningitis and 185 cases of eosinophilic myeloencephalitis have been studied. Living A. cantonensis larvae were found, for the first time in Thailand, in the cerebrospinal fluid of a patient on 3 occasions. Comparative study revealed A. cantonensis to develop better in man than in rat. Two more proven post mortem cases of A. cantonensis infection were recorded. The gross findings in the brains and the size of the microscopic tracks are the 2 points for differentiation between A. cantonensis and G. spinigerum infection. Gnathostoma spinigerum is proved to be an important etiologic agent for the intracranial hemorrhage among the Thai. Experimental work demonstrated that G. spinigerum can invade the central nervous system of mice via oral route of infection.

Table 1 The Prevalence of Typical Eosinophilic Meningitis and Myeloencephalitis in the Studied Provinces during April 1965—March 1969

Location	Typical Form	Myeloencephalitis Form	Total
Bangkok	93	15	108
Ubol	80	128	208
Udorn	26	1	27
Korat	292	12	304
Prachinburi	8	12	20
Saraburi	7	7	14
Lopburi	3	6	9
Pra Buddhabat	25	4	29
Total	534	185	719

Table 2 The Prevalence of Cerebral Vascular Accident of all causes and Cerebral hemorrhage due to Gnathostoma in Saraburi, Pra Buddhabat and Lopburi Hospitals during April 1968—March 1969.

	CVA. (all causes) No. cases	Gnathostoma	
		No. cases	Percent
Bangkok	52	4	7.7
Saraburi	22*	6	27
Pra Buddhabat	81	3	3.7
Lopburi	19	3	15.8
Total	170	16	9.4

* cases admitted during April—October 1968,

Table 3 Measurement of 10 A. cantonensis recovered from C.S.F. of a Thai patient according to day after infection and sex of worm.

Days after infection	Sex	Length (mm)	Average	Width (mm)	Average
8	M	5.3	6.1	.10	0.108
8	M	6.9		.117	
11	M	11.6	11.9	.098	0.108
11	M	12.2		.118	
11	F	8.2	11.2	.125	0.149
11	F	8.4		.118	
11	F	11.3		.133	
11	F	12.1		.182	
11	F	16.2		.191	
18	F	13.61	13.6	.14	0.14

Table 4 Comparative lengths of local (Nakornsawan) strain A. cantonensis in rats' brains and lungs and A. cantonensis found in the cerebrospinal fluids and brains of Thai patients according to days after infection.

Day after infection	Length in mm. in rat	Length in mm. in man
1	0.44	—
3	0.48	—
6	0.92	—
8	1.08	M. 6.1
11	2.84	M. 11.9 F. 11.2
13	4.08	—
15	5.73	—
18	7.83	F. 13.6
21	10.22	—
25	12.59	—
26	—	F. 18.3
28	15.62	—
31	14.41	—
33	16.29*	—
42	24.38*	—

N.B. *in lungs M = Male F = Female

Table 5 The difference in the neuropathology between Angiostrongylus cantonensis and Gnathostoma spinigerum in man

	A. cantonensis	Gnathostoma
1. Gross hemorrhages and necrosis	Rare Minute and few areas	Most constant Massive and multiple sites
2. Gross hemorrhagic tracks	Never seen	Common, multiple
3. Microscopic non-hemorrhagic tracks	Smaller size 20–240 μ (av. 98 μ) Never exceed 250 μ	Bigger size 40–480 μ (av. 225 μ)
4. Microscopic hemorrhagic tracks	Smaller size 65–320 μ (av. 189 μ) Never exceed 350 μ	Bigger size 80–800 μ (av. 388 μ)

Fig. 1 Age distribution of 97 cases of cerebral hemorrhage due to Gnathostoma.

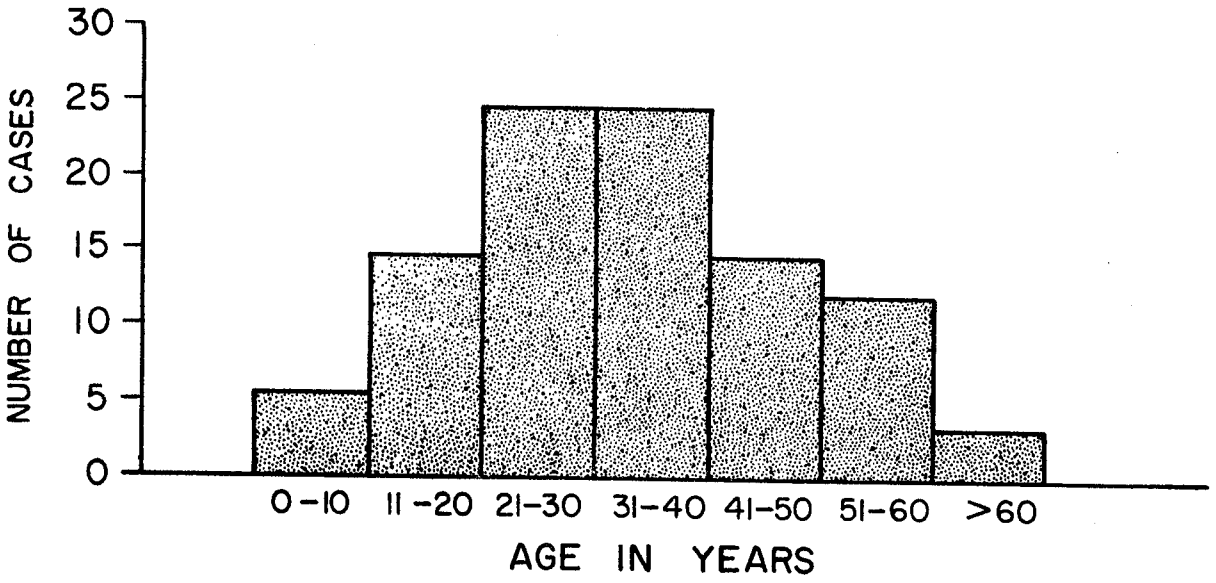
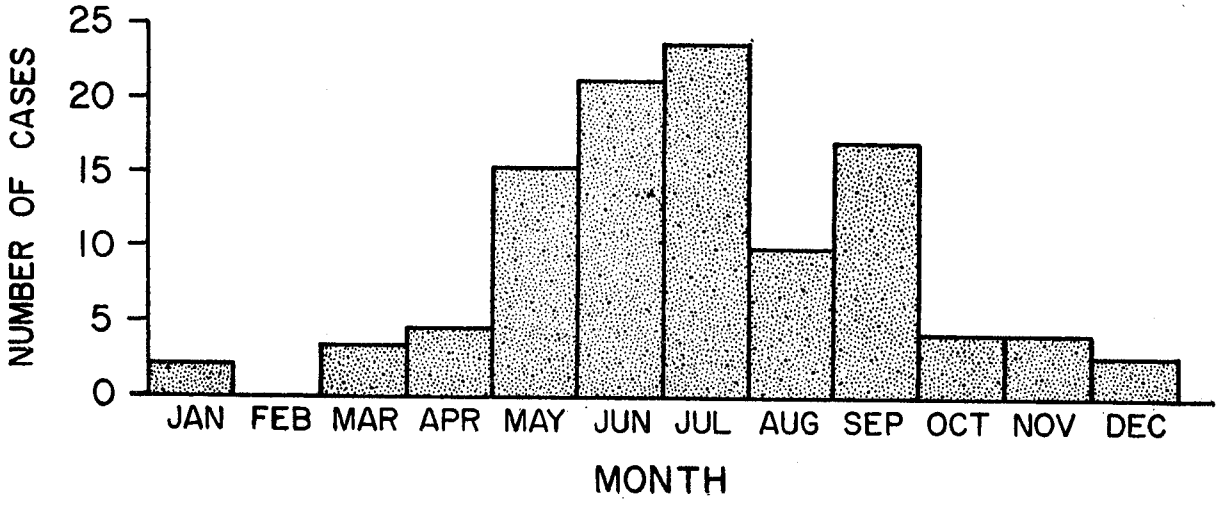


Fig. 2 Distribution of 97 cases of cerebral hemorrhage due to Gnathostoma according to month.



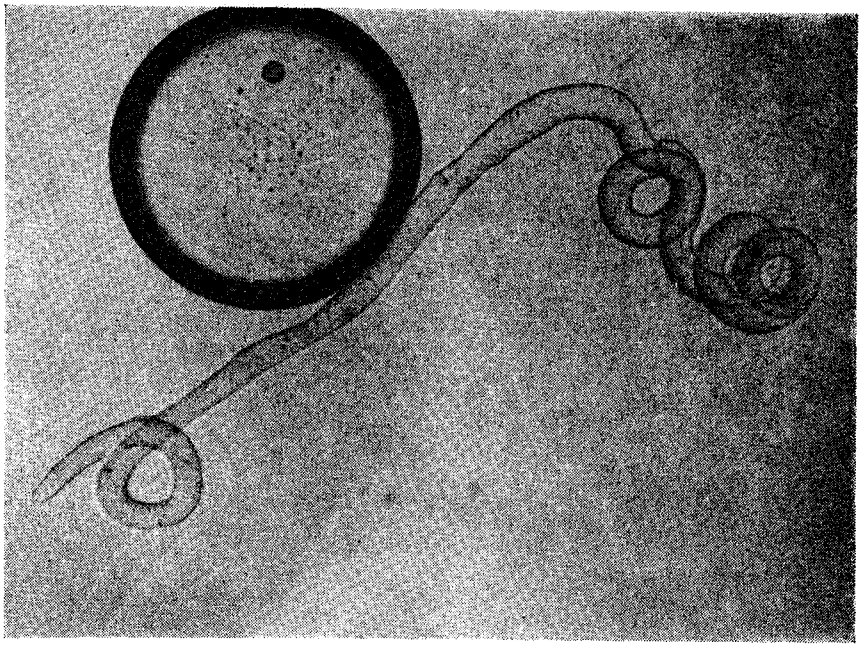


Fig. 3 A male A. cantonensis larva recovered in the cerebrospinal fluid of a Thai patient on the 8th day after infection. (× 28)

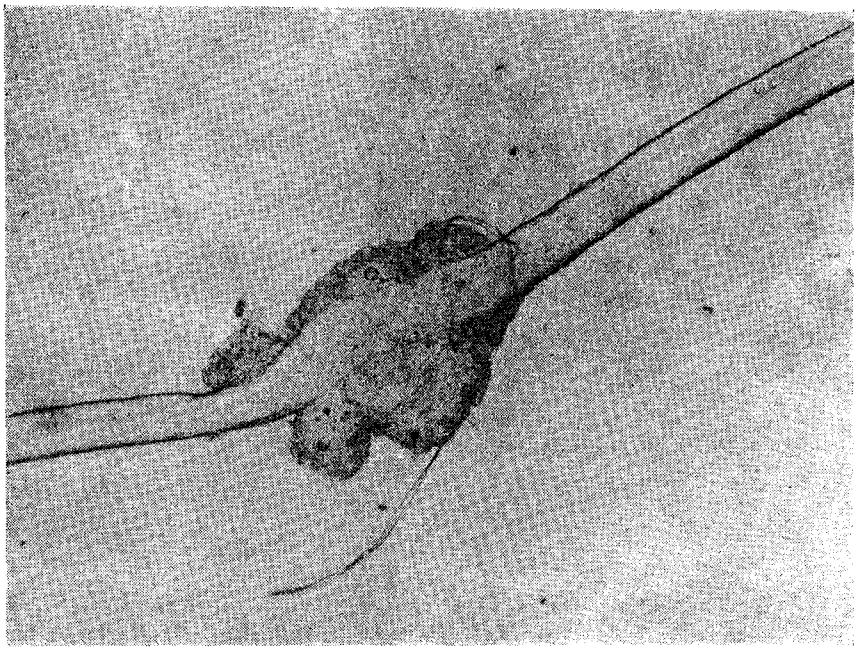


Fig. 4 Clump of white cells noted around the body of a living A. cantonensis recovered on the 11th day after infection. (× 28)

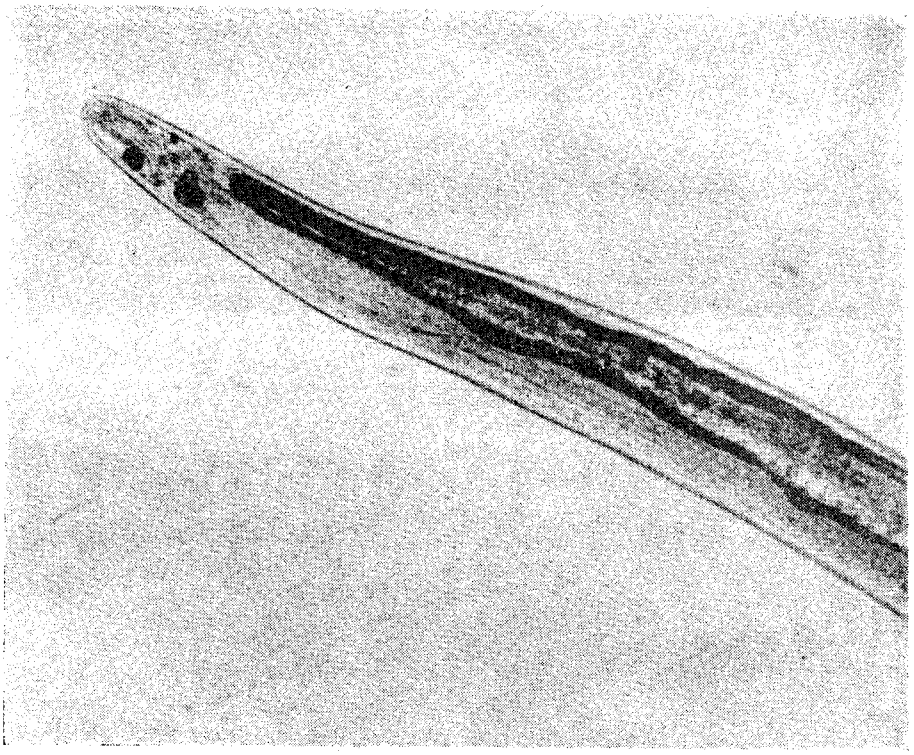
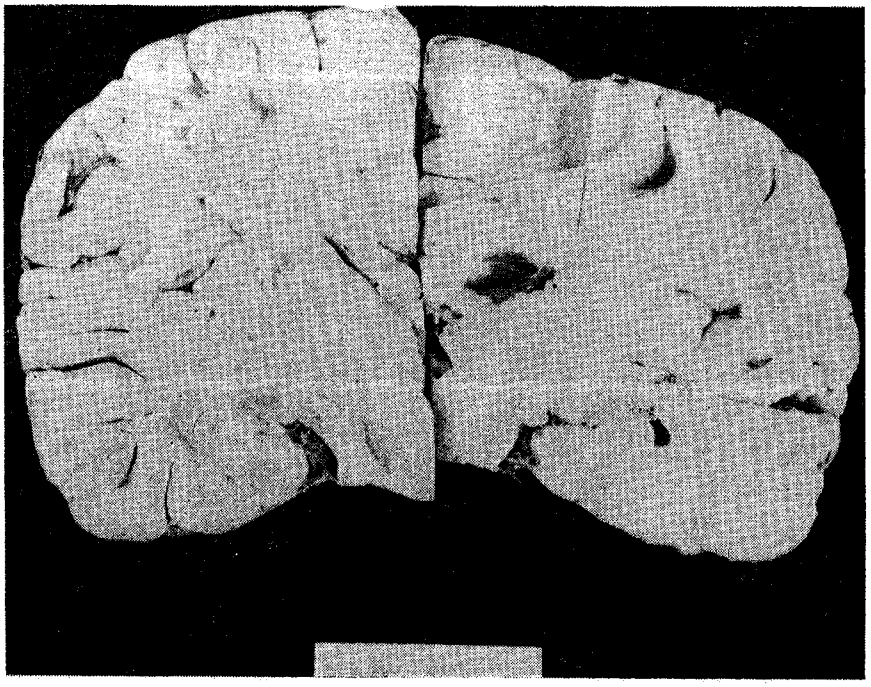
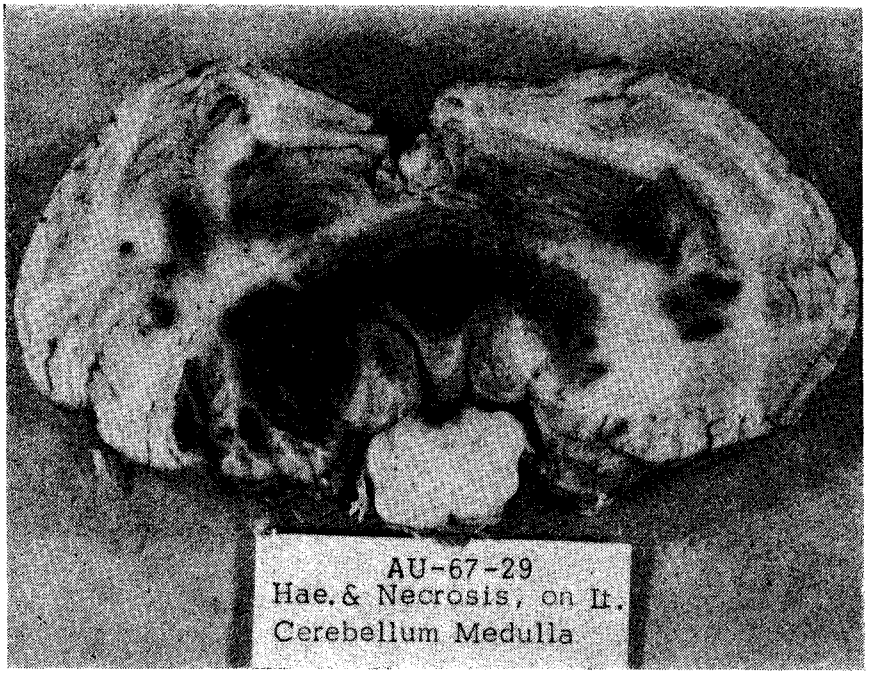


Fig. 5 Head end of morphologically adult A. cantonensis dissected out of the brain of a Thai patient.



A



B

Fig. 6 Comparison of gross neuropathology between A. cantonensis (A) and Gnathostoma Spinigerum (B)