AN ENTEROVIRUS TYPE 70 EPIDEMIC OF ACUTE CONJUNCTIVITIS IN PENINSULAR MALAYSIA, 1980

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INTRODUCTION

Outbreaks of acute viral conjunctivitis due to enteroviruses have been recorded in Malaysia since 1969 when enterovirus type 70 was incriminated for the first time as a cause of acute haemorrhagic conjunctivitis (AHC) throughout the world in 1969-71. The pandemic was reported in Africa, Asia (including Malaysia) and England (Mirkovic *et al.*, 1973). The outbreak in Malaysia then was localised to Kuala Lumpur and Petaling Jaya.

In 1978, another outbreak was reported, also localised to Kuala Lumpur and Petaling Jaya, but this time coxsackievirus A24 (CA24) was found to be the cause (Tan *et al.*, 1980).

In November to December 1980, an epidemic of acute conjunctivitis occurred involving the whole of Peninsular Malaysia, apparently starting in the state of Pahang and assuming extensive proportions in a short time. This paper describes the epidemic and the methods employed in establishing the causal agent.

MATERIAL AND METHODS

Clinical study: The clinical features of 69 patients examined during the epidemic at the Eye Clinic, General Hospital, Kuala Lumpur, were analysed. These patients were all from the Federal Territory and were mostly of lower income group.

Virus isolation: About 70 of the 104 conjunctival scrapings/tear specimens received from the Eye Clinics of the General Hospitals in Kuala Lumpur, Malacca, Ipoh and Seremban were examined for virus isolates in HeLa cell cultures grown in microtitration plates (Yin-Murphy, 1976).

Serology: One pair of sera (acute and convalescent) from the General Hospital in Kuala Lumpur and several single (acute) sera, 12 from Kuala Lumpur, 9 from Malacca, 9 from Seremban and 6 from Ipoh were tested for neutralising antibodies to enterovirus type 70 and CA24. In addition, sera of a control group of non-conjunctival patients, which had been collected for other tests at about the same time as the epidemic and from the same towns, were tested. The method used was the micrometabolic inhibition test.

RESULTS

Table I shows the results of analysis of 69 cases seen in 1980 at the General Hospital, Kuala Lumpur compared with 2133 seen in 1978. Most of the cases were adult male Malays similar to the situation in the outbreak caused by CA24 in 1978. Those under 20 years of age appeared to be relatively spared of the attack during the present outbreak. However, some of them might have been of the "unknown" category in which the age of the patient was not given. In both outbreaks, bilateral involvement predominated over unilateral and there were more moderate/severe cases than mild ones. Congestion was present in all the patients, the majority of whom produced clear watery discharge. Upper respiratory symptoms were noted in 1.8

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TABLE I
EPIDEMIC CONJUNCTIVITIS IN MALAYSIA, 1978 AND 1980

Clinical Features	+ (CA24)	+ + (Enterovirus 70)
Sex:		
Male	71.9	65.2
Female	28.1	34.8
Age (years)		
10 & under	5.3	2.9
11 — 20	22.7	2.9
21 — 30	26.3	27.5
31 — 40	31.7	27.5
41 — 50	10.5	11.6
50 & above	3.5	5.8
*Unknown	0	21.8
Race:		
Malay	50.0	49.3
Chinese	25.9	34.8
Indian	23.5	14.5
Others	1.4	0.6
Involvement		
Unilateral	19.9	8.7
Bilateral	80.1	91.3
Severity		
Mild	39.6	15.9
Moderate/severe	60.4	84.1
Congestion	100.0	100.0
Discharge		
Clear	90.3	84.1
Mucoid	7.0	5.8
Purulent	2.7	10.1
Subconjunctival haemorrhage	2.3	56.5
Chemosis	0	4.3
Pre-auricular lymphadenitis	20.1	46.4
Corneal involvement	9.5	36.2
Upper respiratory symptoms	1.8	1.4

+ 1978 CA24 outbreak. Percentage (Total 2133 cases)
+ + 1980 Enterovirus 70 outbreak. Percentage (Total 69 cases)

* Detail not provided on the request form.

percent (38/2133) in 1978 and 1.4 percent (1/69) in 1980 of cases in both outbreaks.

However, the enterovirus type 70 caused a much higher (though not constant) rate of sub-conjunctival haemorrhage (56.5 percent) (39/69) and corneal involvement (36.2 percent 25/69) than did the CA24 virus (2.3 percent 49/2133 and 9.5 percent 203/2133 respectively).

More cases with purulent discharge were encountered in the present outbreak (10.1 percent 7/69) than in the previous one (2.7 percent 58/2133). Also chemosis, which was not seen with CA24 virus was found in 4.3 percent 3/69 of the cases caused by enterovirus 70. Pre-auricular lymphadenopathy was more frequently noted in this outbreak (46.4 percent 32/69) than in the previous one (20.1 percent 429/2133) probably due to more cases with the secondary bacterial complications, the acute infection of which lasted for more than one to three weeks in a number of patients.

Virus isolates were not obtained from any of the 70 eye specimens although 2 to 3 blind passages were performed for most of them. Several specimens showed minimal CPE changes in the HeLa cell cultures but the agent was lost on subsequent passages. Only one pair of sera was received (from the General Hospital, Kuala Lumpur). The first sample (4th day) gave a neutralising antibody titre of 1:40 and the second (14th day), 1-160 against enterovirus type 70. Both were negative to CA24. Based on this, a tentative diagnosis of an enterovirus type 70 outbreak was made and reported.

On not receiving further corresponding (convalescent) sera of the other single (acute) specimens from the hospitals, it was decided, nevertheless, to test the single specimens and compare them with a control group of sera collected during the same period from a representative number of non-conjunctival patients from the same towns. Table 2 shows that 43.2 percent (16/37) of the conjunctival patients had enterovirus 70 antibodies ranging from 1:10 to 1:40 compared with 21.4

TABLE II
SEROLOGICAL RESPONSE IN PATIENTS WITH ACUTE CONJUNCTIVITIS, 1980
(COMPARED WITH THE 1978 (CA24) OUTBREAK)

TOWN	Enterovirus type 70				Coxsackie A 24			
	Patients		Control		Patients		Control	
	No. Exam	Pos.	No. Exam	Pos.	No. Exam	Pos.	No. Exam	Pos.
Kuala Lumpur	13*	9	18	3	13	0	18	0
Malacca	9	7	9	3	9	0	9	0
Seremban	9	0	9	3	9	1	9	0
Ipoh	6	0	6	0	6	0	6	0
Total	37	16 (43.2%)	42	9 (21.4%)	37	1 (2.7%)	42	0

* One of these patients submitted paired specimens which showed a significant antibody rise to enterovirus type 70, but was negative to CA24.

percent (9/42) of the control group. This difference is significant ($P = <.05$). Minimal or no antibodies to CA24 (2.7 percent) were found in the two groups.

DISCUSSION

This study shows the importance of submitting *paired* sera of patients for serological tests as virus isolation cannot be relied upon especially when the specimens for culture have to be transported from some distance to the laboratory. In the investigation of this outbreak it was fortunate that some of the acute sera were collected at a time when the antibodies became detectable, thus helping to establish the identity of the causal agent. The negative results obtained with the sera of the patients from Seremban and Ipoh probably indicates that the sera had been collected before any antibody response could be detected. The difficulty in isolating enterovirus type 70 was also experienced in Ghana (Chatterjee *et al.*, 1970) and Nigeria (Parrot, 1971) during the pandemic of 1969-71.

Clinically, enterovirus type 70 appears to cause a more severe form of conjunctivitis then CA24 virus, with a greater frequency of sub-conjunctival haemorrhage, corneal involvement and secondary bacterial complications, and the infection tends to spread faster and more extensively than with CA24.

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REFERENCES

Chatterjee, S., Quarcoopome, C.O. & Apenteng, A (1970). An epidemic of acute conjunctivitis in Ghana. *Ghana Medical J.*, **9**, 9-11.

Mirkovic, R.R., Kono, R., Yin-Murphy, M., Sohier, R., *et al.*, (1973). Enterovirus type 70: the aetiologic agent of pandemic acute conjunctivitis. *Bull. Wld. Hlth. Org.*, **49**, 341-346.

Parrott, W.F. (1971) An epidemic called Apollo. An outbreak of conjunctivitis in Nigeria. *Practitioner*, **206**, 253-255.

Tan. Dora S.K., Yin – Murphy, M. & Kandiah, S. (1980). An outbreak of acute conjunctivitis caused by Coxsackievirus A24 in Kuala Lumpur, Malaysia, 1978. *Southeast Asian J., Med. & Pub. Hlth. trop.* **11**, 24-25.

Yin-Murphy, M. (1976) Simple tests for the diagnosis of picornavirus epidemic conjunctivitis (acute haemorrhagic conjunctivitis). *Bull. Wld. Hlth. Org.* **54**, 675-679.