

ECHOVIRUS TYPE 4 OUTBREAK IN NORTHERN IRELAND DURING 1970-71

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AN extensive outbreak of Echovirus type 4 took place during 1970-71 in Northern Ireland. Echovirus type 4 is not only a rare virus to isolate from patients but this was also the third major enterovirus outbreak in Northern Ireland during the past four years. The other outbreaks were associated with Echovirus type 6 during 1968 (Connolly and O'Neill, 1970) and Coxsackie A9 virus during 1970 (Connolly and O'Neill, 1971).

MATERIALS AND METHODS

Faeces, CSF, throat swabs and acute and convalescent sera were obtained from patients with aseptic meningitis while faeces and/or throat swabs were obtained from other cases.

Primary rhesus monkey kidney cell cultures were used for virus isolation. At the beginning of the outbreak the first virus isolates could not be typed using the Echovirus diagnostic serum pools supplied by the Standards Laboratory, Central Public Health Laboratory London. The first virus isolates were typed using an Echovirus type 4 (strain Pesascek) neutralising antiserum from Microbiological Associates Inc. which was not included in the Echovirus diagnostic serum pools. It was found that the Echovirus type 4 (strain Du Toit) neutralising antiserum supplied by the Standards Laboratory when used at the recommended dilution of 1:640 would not neutralise our isolates, but worked satisfactorily when used at a final dilution of 1:40. Acute and convalescent sera were available from 62 patients from whom virus was not isolated and who had aseptic meningitis during the period of the Echovirus type 4 outbreak. The convalescent sera were tested at a final dilution 1:20 against 100 TCD₅₀ of Echovirus type 4 (strain Du Toit) in a four hour neutralisation test at 37°C. and the acute and convalescent sera of those which had antibody were then titrated. The sera from all aseptic meningitis patients were also tested for rising titres of antibody against mumps, measles, herpes simplex, louping ill and lymphocytic choriomeningitis viral antigens using the overnight complement fixation test at 4°C. (Bradstreet and Taylor, 1962).

RESULTS

In Northern Ireland during 1970-71 Echovirus type 4 was isolated from 169 patients. Echovirus type 4 was isolated from the faeces of 154 patients and from the throat of 33 patients. The virus was isolated from the CSF of 33 patients (19%) with aseptic meningitis. Antibody could not be demonstrated in acute and convalescent sera from three patients from whom Echovirus type 4 was isolated when 100 TCD₅₀ of an Echovirus type 4 which had been isolated from the CSF of a patient in the current outbreak was used in the neutralisation test. However, four fold or greater rises in antibody were found in these three patients when TCD₅₀ of Echovirus type 4 (Du Toit strain) was used in the neutralisation test. Sixty-two

patients with aseptic meningitis during the current outbreak from whom Echovirus type 4 was not isolated were tested and four fold or greater rises in Echovirus type 4 neutralising antibody were found in fourteen patients making a total of 183 patients diagnosed with Echovirus type 4 infection. A five year old boy with aseptic meningitis had serological evidence of recent infection with herpes simplex and mumps virus and Echovirus type 4 was also isolated from his throat and faeces.

The number of patients with Echovirus type 4 infection and the month of onset of their illness are shown in Table I.

TABLE I

Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May.	June	July	Aug.	Sept.	Oct.	Nov.
3	—	4	5	7	17	29	28	42	19	16	12	1

The outbreak began in November 1970 and ended in November 1971 while 99 cases (54 per cent) occurred in May, June and July 1971 with a peak incidence during July. One hundred and twenty-six patients (69 per cent) lived in Belfast and surrounding suburbs, an area which has a population of approximately 500,000. The clinical attack rate for that area was 25 per 100,000 population. There were 57 patients (31 per cent) outside this area in Co. Antrim (25), Co. Armagh (14), Co. Tyrone (8), Co. Down (6), and Londonderry Borough (4). The clinical attack rate for Northern Ireland as a whole was 12 per 100,000 population.

The illness associated with the Echovirus type 4 infections and the age and sex of the patients are shown in Table II.

TABLE II

Illness, Age and Sex of patients with Echovirus type 4 infections during 1970/71

Illness	Age in Years						Sex		Total	
	<1	1-4	5-9	10-14	15-19	>20	Male	Female	Number	Per cent
Aseptic Meningitis	2	12	48	43	28	39	97	75	172	94.0
Respiratory	2	2	1	—	—	1	3	3	6	3.3
Pyrexial	3	1	—	1	—	—	3	2	5	2.7
All Clinical Categories	7	15	49	44	28	40	103	80	183	100.0

One hundred and seventy-two patients had aseptic meningitis which was the predominant illness accounting for 94 per cent of all cases. Three patients had a rash associated with their illness which included a two-month-old girl and an eleven-month-old boy with pyrexia and a three-month-old boy with aseptic meningitis. The respiratory cases included two three-month-old girls and a four-year-old boy with pneumonia, a one-year-old boy and an eight-year-old girl with pharyngitis, while a twenty-six-year-old man had pleurodynia. Three of the five patients with a pyrexial illness were less than one-year-old. There were no deaths.

The outbreak was confined mainly to children with over half the cases occurring in the 5—14-year-old age group and more males than females were affected. The youngest patient in the outbreak was two-months-old. In the aseptic meningitis group males predominated and the 5—14-year-old group was affected most. The youngest patient with aseptic meningitis was a three-month-old boy and the oldest was a 46-year-old woman.

There were nine families where two or more members developed aseptic meningitis associated with Echovirus type 4 infection as shown in Table III.

TABLE III
Family outbreaks of Echovirus type 4 Aseptic Meningitis in Belfast 1971

<i>Family No.</i>	<i>Date of onset</i>	<i>Age in years</i>	<i>Sex</i>
1	Jan. 18	7	M
	20	6	M
2	April 17	6	M
	18	5	M
3	April 28	20	F
	May 4	11	M
4	May 9	7	F
	27	5	M
5	May 31	11	F
	31	13	M
6	July 1	7	M
	1	27	M
7	Sept. 9	16	M
	10	9	M
8	Sept. 13	11	F
	20	14	F
	21	5	M
9	Oct. 16	7	F
	22	12	M
	25	15	F
	31	10	M

Two children in each of five families developed aseptic meningitis. In family number 6 a father and son and in family number 3 a boy and his adult sister were affected. In family number 8 three children were involved while in family number 9, four children developed aseptic meningitis. Within each family the onset of their illnesses was closely associated in time.

Apart from the family outbreaks there were outbreaks of Echovirus type 4 infection in 14 separate streets as shown in Table IV.

TABLE IV
Street outbreaks of Echovirus type 4 Aseptic Meningitis 1971

<i>Street No.</i>	<i>Date of Onset</i>	<i>Age in years</i>	<i>Sex</i>	<i>Location</i>
1	April 14	29	M	Suffolk Co. Antrim
	Aug. 3	1 ⁽¹⁾	M	
2	April 28	27	F	Dundonald Co. Down
	June 25	4	F	
3	May 10	20	F	Castlewellan Co. Down
	July 22	14	M	
4	May 23	5	M	Belfast
	May 31	3	M	
	June 4	14	M	
5	May 24	4	F	Belfast
	May 28	7	F	
6	May 25	2/12 ⁽²⁾	F	Belfast
	June 20	17	M	
7	June 29	14	M	Armagh
	July 7	14	M	
8	July 4	7	F	Rathcoole Co. Antrim
	July 26	6	F	
	July 27	5	M	
9	July 13	5/12 ⁽³⁾	M	Belfast
	Aug. 24	12	F	
10	July 17	8	F	Belfast
	July 18	6	M	
11	July 19	4	M	Belfast
	Aug. 7	5	M	
12	July 25	9	M	Belfast
	Sept. 14	14	M	
13	Aug. 13	8	F	Belfast
	Aug. 15	9	F	
14	Oct. 4	26	F	Belfast
	Oct. 8	11	F	

(1) Child had pharyngitis and convulsions only.

(2) Child had pyrexia and rash only.

(3) Child had pyrexia and vomiting only.

Two children in each of six streets had Echovirus type 4 infection and in four streets an adult and a child were affected. Three children in each of two streets had aseptic meningitis. In street number 9, four children (two of them being in family number 6) had Echovirus type 4 infections while in street number 12, six children had aseptic meningitis (four of them being in family number 9). Fifty-one patients (28 per cent) were involved in family and street outbreaks of Echovirus

type 4 infection. It was also observed from the patients' addresses that many individual cases of aseptic meningitis lived in adjoining streets.

DISCUSSION

Usually Echovirus type 4 is one of the more uncommon types isolated in the United Kingdom, there being only fifty-four infections reported in the five years 1966-70 (Brit. med. J., 1971a). During 1970-71 the two largest outbreaks began in Teeside during September 1970 and in Belfast during November 1970 (Brit. med. J., 1971b).

The Echovirus type 4 outbreak in Northern Ireland was typical of enterovirus infections in that it had a peak incidence during the summer months and over half the cases were in children aged 5-14 years. Proportionally more patients were affected in the older 10-19 year age groups in this outbreak when compared to the previous Echovirus type 6 and Coxsackie type A9 outbreaks. The clinical attack rate for Northern Ireland as a whole was 12/100,000 population which was eight fold higher than the rest of the United Kingdom, but direct comparisons are difficult because many areas in the rest of the United Kingdom were spared.

The predominant illness associated with the Echovirus type 4 outbreak in Northern Ireland was aseptic meningitis accounting for 94 per cent of all cases. The patients investigated in this outbreak were, however, highly selected in that their illnesses were severe enough to require admission to hospital. There were probably many more minor illnesses, and subclinical infections in the community associated with Echovirus type 4.

Enteroviruses spread by direct person to person oral transfer of human faeces or from the respiratory tract, and this is substantiated by the nine family outbreaks of aseptic meningitis where close contact between individuals is known to occur. The outbreaks of aseptic meningitis and other illnesses in fourteen streets could be explained on the basis of play-contacts. The individual cases of aseptic meningitis which occurred in adjoining streets could be explained either on the basis of play-contacts or possibly contact at school.

Our results show that only the Du Toit strain of Echovirus type 4 was neutralisable and not the strain isolated from patients in the outbreak. Barron and Karzon (1961) investigated an epidemic of Echovirus type 4 aseptic meningitis and found that attempts to show rises of neutralising antibody in patients' sera with prototype virus (Pesascek strain) or patients' own isolate were generally unsuccessful when used in a tube neutralisation test whereas the Du Toit strain was neutralisable. Wallis and Melnick (1967) showed that virus aggregation was the cause of the non-neutralisable persistent fraction of Echovirus type 4 which constituted 30 per cent of the infective units of the unfiltered Pesascek strain but only 0.1 per cent of the antigenically related Du Toit strain.

SUMMARY

In Northern Ireland 183 patients were shown to be infected with Echovirus type 4 between November 1970 and November 1971. The peak incidence was in July 1971 and the outbreak was largely confined to Belfast and its environs. One hundred and three males and eighty females were affected and over half the patients

were in the 5—14-year-old age group. One hundred and seventy-two patients (94 per cent) had aseptic meningitis. There were nine family outbreaks and fourteen street outbreaks where two or more people in each family or street had aseptic meningitis. Individual cases of aseptic meningitis also occurred in adjoining streets. Neutralising antibody in patients' sera could only be demonstrated using the Du Toit strain of Echovirus type 4.

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