COXSACKIE A9 VIRUS OUTBREAK IN NORTHERN IRELAND DURING 1970

by

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THE LARGEST outbreak of Coxsackie A9 virus infection yet experienced in Northern Ireland took place during 1970 and a disproportionately greater number of cases occurred in Northern Ireland compared with the rest of the United Kingdom (British Medical Journal, 1970a).

MATERIALS AND METHODS

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

Primary rhesus monkey kidney cell cultures were used for virus isolation and isolated viruses were typed with Coxsackie A9 neutralizing serum supplied by the Standards Laboratory, Central Public Health Laboratory, London.

Acute and convalescent sera from aseptic meningitis cases from whom virus had not been isolated and who were negative when screened serologically in the complement fixation test against mumps, measles, herpes simplex, lymphocytic choriomeningitis and louping ill viral antigens were tested for Coxsackie A9 virus neutralizing antibody. Sera were inactivated at 56°C for 30 minutes then serial dilutions were mixed with equal volumes of 200 TCD₅₀ of Coxsackie A9 virus which had been isolated from the CSF of a patient in the current outbreak. The virus-serum mixtures were left for 2 hours at 37°C before inoculation.

RESULTS

In Northern Ireland during 1970, 123 patients had Coxsackie A9 virus infection diagnosed in the laboratory. Coxsackie A9 virus was isolated from 119 patients. This virus was isolated from the CSF of 54 patients (51 per cent) with aseptic meningitis. Coxsackie A9 virus was also isolated from the throat of 60 patients and from the faeces of 93 patients. It was observed that Coxsackie A9 virus was isolated more quickly from the CSF or throat swab than from faeces obtained from the same patient. Serological tests on 40 additional patients with aseptic meningitis showed that four had an eightfold or greater rise in Coxsackie A9 neutralizing antibody which indicated recent infection while 28 had equivalent titres in their acute and convalescent sera which indicated past infection with this virus.

The number of patients with Coxsackie A9 virus infection and the month of onset of their illness are shown in Table I.

|     | Mar. | Apr. | May | June | July | Aug. | Sept. | Oct. | Nov. |
|-----|------|------|------|------|------|------|-------|------|------|
|     | 1    | 2    | 28   | 44   | 23   | 19   | 3     | 2    | 1    |

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The outbreak began in March and ended in November while 114 cases (93 per cent) occurred between May and August with a peak incidence during June. One hundred and six patients (86 per cent) lived in Belfast or in surrounding suburbs and towns within a ten mile radius, an area which has a population of approximately 500,000. The clinical attack rate in that area was 21 per 100,000 population. There were 17 patients (14 per cent) outside this area. These patients were scattered widely in Co. Antrim (1), Co. Down (1), Co. Armagh (5), Co. Tyrone (4) and Co. Londonderry (6). The clinical attack rate for Northern Ireland as a whole was 8 per 100,000 population.

The illnesses associated with the Coxsackie A9 infections and the age and sex of the patients are shown in Table II.

### Table II

| Illness                  | <1 | 1-4 | 5-9 | 10-14 | 15-19 | 20+ | Male | Female | Number | Per cent |
|--------------------------|----|-----|-----|------|------|-----|------|--------|--------|----------|
| Aseptic Meningitis       | 1  | 14  | 37  | 22   | 8    | 24  | 73   | 33     | 106    | 86.2     |
| Respiratory              | —  | 3   | 2   | 1    | —    | 1   | 3    | 4      | 7      | 5.7      |
| P.U.O. & Myalgia         | 2  | 2   | 2   | —    | —    | —   | 4    | 2      | 6      | 4.9      |
| Gastro-intestinal        | 1  | —   | 1   | —    | —    | —   | 2    | —      | 2      | 1.6      |
| Probable excreters       | 2  | —   | —   | —    | —    | —   | 1    | 1      | 2      | 1.6      |
| All clinical categories  | 4  | 21  | 42  | 23   | 8    | 25  | 83   | 40     | 123    | 100.0    |

Aseptic meningitis was the predominant illness associated with Coxsackie A9 virus infection in Northern Ireland accounting for 86 per cent of all cases. Eight patients had a rash associated with their illness which included four patients with aseptic meningitis, two patients with P.U.O. and one patient each with vomiting and pharyngitis. In addition one other child had a measles rash in association with his Coxsackie A9 infection. The respiratory cases included five patients with pharyngitis, one patient with pleurodynia and another patient with bronchitis and cough. One 3 year old boy had such severe myalgia in his leg muscles that he had difficulty in walking. The probable excreters included a child with an acute onset haemolytic anaemia and another child who was admitted as a "feeding problem". There were no deaths associated with Coxsackie A9 virus infections during 1970.

The outbreak was confined mainly to children with over half the cases occurring in those under the age of 10 years. The youngest patient was 2 months old and the oldest was 36 years old. In the aseptic meningitis group there were over twice as many males as females affected and the 5–9 year old age group was affected most. The youngest patient with aseptic meningitis was a boy of 9 months and the oldest was a woman of 36 years. Two boys had double viral infections confirmed virologically associated with their aseptic meningitis; one had measles virus infection and the other had mumps virus infection in association with their Coxsackie A9 infections.
There were 8 families where two or more members developed aseptic meningitis associated with Coxsackie A9 virus infection as shown in Table III.

**TABLE III**

*Family Outbreaks of Coxsackie A9 Virus Aseptic Meningitis 1970*

| Family No. | Date of onset | Age in years | Sex | Town          |
|------------|---------------|--------------|-----|---------------|
| 1          | 1 May         | 4            | F   | Belfast       |
|            | 6 May         | 3            | F   |               |
| 2          | 10 May        | 11           | M   | Belfast       |
|            | 22 May        | 7            | F   |               |
| 3          | 13 June       | 5            | M   | Hillsborough, |
|            | 13 June       | 11           | M   | Co. Down      |
|            | 19 June       | 21           | F   |               |
| 4          | 10 July†      | 36           | F   | Belfast       |
|            | 17 July*      | 8            | F   |               |
|            | 18 July       | 8            | M   |               |
|            | 19 July       | 7            | F   |               |
| 5          | 7 August      | 12           | M   | Limavady,     |
|            | 18 August     | 6            | F   | Co. Londonderry|
| 6          | 12 August     | 9            | M   | Londonderry   |
|            | 13 August     | 10           | F   |               |
| 7          | 24 August     | 11           | M   | Belfast       |
|            | 29 August     | 8            | M   |               |
| 8          | 29 September  | 8            | M   | Armagh        |
|            | 29 September  | 9            | F   |               |

†Mother of the two affected children.
*Not a member of family 4 but lived in same street and played frequently in their house.

Two children in each of six families developed aseptic meningitis, while in family number 3, three persons developed aseptic meningitis. In family number 4, the mother and a neighbouring child also developed aseptic meningitis. In families number 3 and 8, two children became ill on the same day which may indicate that both children became infected at the same time from an unknown third person, while in family number 6 there was only one day between the onset of their illnesses. The interval between the onset of illness in the two children in the other families was 5–12 days.

**DISCUSSION**

The most common Coxsackie A type identified in diagnostic virus laboratories in the United Kingdom is Coxsackie A9 and the prevalence was particularly high in 1963–4, 1966–7 and 1969–70 (British Medical Journal, 1970b).

The Coxsackie A9 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 under 10 years old. Although 220 patients with Coxsackie
A9 infections were reported from the United Kingdom during 1969, only 3 patients came from Northern Ireland, the last case being in October, 1969; an interval of 5 months before the onset of the present outbreak. A three month old boy with hyperpyrexia and convulsions died in February 1969 and Coxsackie A9 virus was isolated from his liver and gut at post mortem, but there were no deaths associated with Coxsackie A9 infection during 1970 in Northern Ireland.

There were 259 Coxsackie A9 infections reported in the United Kingdom during 1970 (Private communication, Public Health Laboratory Service) and about half of these came from Northern Ireland. The clinical attack rate for Northern Ireland as a whole was 8 per 100,000 population compared with 0.25 per 100,000 population for the rest of the United Kingdom. This 32 fold difference in clinical attack rates may to some extent be explained by the fact that the rest of the United Kingdom had had an increased prevalence of Coxsackie A9 infections during 1966-67 and 1969 with a subsequent increase in the number of immune persons in the population during 1970. The patients investigated in this outbreak were highly selected in that their illnesses were severe enough to require admission to hospital. Undoubtedly there were many more minor illnesses and subclinical infections in the community associated with Coxsackie A9 virus.

Eighty-six per cent of patients with Coxsackie A9 infection in Northern Ireland had aseptic meningitis and this predominance contrasts with 27 per cent of children and 61 per cent of adults reported to have central nervous system involvement associated with Coxsackie A9 infection in the United Kingdom during 1969 (British Medical Journal, 1970b). In most outbreaks of viral meningitis investigated in Northern Ireland including the present outbreak, twice as many males as females were involved.

It was of interest that 8 families had two or more cases of aseptic meningitis associated with Coxsackie A9 infection in each family. Since spread of enteroviruses is by direct person to person oral transfer of human faeces or from the respiratory tract it follows that family infections are common though clinical illness is usually rare. The fact that Coxsackie A9 virus was isolated earlier from CSF and throat swabs rather than faeces probably means that the virus was of higher titre in the CSF or throat so that respiratory rather than faecal spread may have been of importance in this outbreak.

**SUMMARY**

During the summer months of 1970 there was an outbreak of Coxsackie A9 virus infection in Northern Ireland which was confined largely to Belfast and its environs. The clinical attack rate was 32 times higher in Northern Ireland than the rest of the United Kingdom. One hundred and twenty-three patients were diagnosed. Males were affected twice as often as females and over half the patients were children under the age of 10 years. One hundred and six patients (86 per cent) had aseptic meningitis and there were 8 family outbreaks where two or more people in each family had aseptic meningitis.

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