Predominant enteroviral serotypes causing meningitis

Philip J Atkinson, Mike Sharland, Helen Maguire

Abstract

All enteroviral reports to the Public Health Laboratory Service from 1975 to 1994 which had been proved by culture were analysed. Of the 40 366 isolates, 5741 reports (14%) were from cultures of cerebrospinal fluid. The groups and serotypes accounting for the largest number of cerebrospinal fluid isolates were A9, E7, E9, E11, E19, and E30, accounting for 70% of all cultured isolates of cerebrospinal fluid. It may be possible to prevent most cases of viral meningitis in the UK with the development of an enteroviral vaccine. (*Arch Dis Child* 1998;78:373-374)

Keywords: enteroviruses; cerebrospinal fluid; viral meningitis

Public Health Laboratory Service, Communicable Disease Surveillance Centre (Thames), London
P J Atkinson
H Maguire

Paediatric Infectious Disease Unit, St George's Hospital, London
M Sharland

Correspondence to:
Philip J Atkinson, Public Health Laboratory Service, Communicable Disease Surveillance Centre (Thames), 40 Eastbourne Terrace, London W2 3QR.

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Enteroviruses consist of five groups and 67 different serotypes: group A coxsackie (23 serotypes), group B coxsackie (six serotypes), echoviruses (31 serotypes), polioviruses (three serotypes), and the newer enteroviruses 68-71 (four serotypes). Enteroviruses can cause a wide variety of clinical diseases. They are recognised as a leading cause of acute febrile illness in young children¹ and are now the most common cause of viral meningitis in England and Wales following the introduction of the mumps vaccine in 1988. Enteroviruses can also cause conjunctivitis; hand, foot, and mouth disease; exanthemata and enanthemata; pleurodynia; neonatal infections; and upper and lower respiratory tract infections. Individual enteroviral serotypes do not show clear associations with particular disease syndromes, but do have

a propensity to cause particular symptoms.² The study reported here examined enterovirus serotypes associated with meningitis which were reported over a 20 year period in England and Wales.

Methods

Data were analysed for the 20 year period 1975 to 1994 of non-polio enteroviral infections confirmed by culture and reported to the Public Health Laboratory Service (PHLS) Communicable Disease Surveillance Centre (CDSC) from laboratories in England and Wales. A positive isolate from cerebrospinal fluid was taken to indicate the presence of viral meningitis. Age specific rates of infection were calculated using Office for National Statistics (ONS, formerly Office of Population Censuses and Surveys) 1985 mid-year population estimates.

Results

Over the 20 year period 1975 to 1994 there were 40 366 isolates proved by culture. Of these, 4024 (10%) were coxsackie A, 11 714 (29%) coxsackie B, and 24 628 (61%) echoviruses. The number of annual reports decreased over time from 3153 in 1975 to 777 in 1994. Strong seasonal trends can be seen in each year; 71% of reports had specimen dates between July and December. There was a male predominance (57% male, 41% female, 2% unknown sex). When analysing all culture reports except those from cerebrospinal fluid, the highest rates of positive reports were seen in children aged less than 1 year (over 65 reports/100 000 children), peaking in the 1-2 month age range (127 reports/100 000 children) (fig 1).

Of the 40 366 isolates proved by culture, 5741 (14%) were from cerebrospinal fluid. Of the isolates from cerebrospinal fluid, 673 (12%) were coxsackie A, 790 (14%) were coxsackie B, and 4278 (75%) were echoviruses. There was again a male dominance (54% male, 44% female, 2% unknown sex). Reports of cerebrospinal fluid isolates remained at about 15% of all isolates throughout the 20 year period, despite large enteroviral outbreaks. The highest rates of cerebrospinal fluid isolates were again seen in children aged less than 1 year (over 2/100 000) and peaked in the 0-1 month age range (23/100 000) (fig 1). Groups and serotypes accounting for the largest number of cerebrospinal fluid isolates were A9, E7, E9, E11, E19, and E30. Together these accounted for 70% of all isolates cultured from cerebrospinal fluid (table 1).

Figure 1 Rate per 100 000 population by age of cerebrospinal fluid and non-cerebrospinal fluid non-polio enteroviral isolates reported to the PHLS CDSC from 1975 to 1994.

Table 1 Largest number of non-polio enteroviral serotypes in cerebrospinal fluid (CSF) reported to the PHLS CDSC from 1975 to 1994

Serotype	No of CSF isolates	No of non-CSF isolates	Percentage (rank) of all CSF isolates
A9	597	1 888	10 (5)
E7	464	2 083	8 (6)
E9	741	1 592	13 (2)
E11	898	4 117	16 (1)
E19	671	1 290	12 (3)
E30	639	1 904	11 (4)
Total of six serotypes	4010	12 874	70

Discussion

The use of a positive cerebrospinal fluid specimen as an indicator of meningitis has the advantage of providing a consistent case definition, but is influenced by the trend in clinicians performing lumbar punctures. Opinions vary about whether this has increased or decreased.

The decrease in enteroviruses over the 20 year period may be a result of fewer laboratories reporting to the PHLS, fewer cerebrospinal fluid tests being performed, or a true reduction in disease. Laboratories diagnosing enteroviral infection do not always confirm the group and serotype. Reports to the PHLS are of isolates where at least the group is known (H Maguire, P Atkinson, M Sharland, J Bendig, unpublished results).

Between 1982 and 1994 there were 4400 notifications of viral meningitis in England and Wales reported to the ONS, compared with 3100 enteroviral cerebrospinal fluid isolates reported to PHLS CDSC over the same period (P Horby, H Maguire, P Atkinson, unpublished results). Annual figures vary between the two sources, but overall the totals and broad trends are similar. Despite the problems of under notification, possible under reporting of laboratory results, positive specimens other than those from cerebrospinal fluid, and the lack of laboratory confirmation in children with aseptic meningitis, this similarity suggests the

cerebrospinal fluid data are representative of viral meningitis in England and Wales.

The distribution of enteroviral serotypes is influenced by the ease of laboratory isolation. For example, only coxsackie A serotypes A9, A7, A16, A21, A24, and, occasionally, A16 are easily recoverable by standard cell culture systems.

Our "top" six serotypes with the highest number of cerebrospinal fluid isolates match well with equivalent data from other studies and give an indication of the burden of illness associated with certain enteroviruses.²⁻⁴ It is possible that other neurotropic enteroviruses which are less easily isolated may contribute to a greater degree than is apparent here. In addition, enteroviruses which were not epidemic during the 20 year period may potentially cause disease in an epidemic period in the future.

We believe that the identification of particular enteroviral serotypes frequently causing meningitis is helpful and raises the question of vaccine development. Current levels of enteroviral disease, peaking in neonates with low mortality, suggest that the vaccine would currently be given a low priority in the development of childhood vaccines. With the advent of a vaccine against most bacterial causes of meningitis, and progress with a meningococcal group B vaccine rapidly advancing, there may be an increased role for enteroviruses in the future and thus vaccine development would become a greater priority.

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