



# An Understanding of the True Burden of Enterovirus Meningitis may require a Review of Clinical and Laboratory Case Criteria



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## Background

- Enteroviruses account for over seventy per cent of viral meningitis notifications in Ireland.
- The burden of enterovirus meningitis weighs heavily on the paediatric population, with over 40% of all cases occurring in infants under one year.
- Current case definitions for viral meningitis in Ireland require the presence of a cerebrospinal fluid (CSF) white cell count (WCC) pleocytosis for confirmed or probable laboratory criteria to be met.<sup>1</sup>
- However, it has been reported in the literature that there is an absence of CSF pleocytosis in up to 30 per cent of infants with enterovirus meningitis<sup>2,3</sup>
- As such, some laboratories may not refer CSF samples for further microbiological testing in the absence of a raised WCC.
- Consequently, cases of enteroviral meningitis such as these would be neither diagnosed nor captured by viral meningitis reporting systems.

## Materials and Methods

- Data were collected from the records of children attending a paediatric or maternity hospital in Dublin, Ireland between 2010 and 2014.
- CSF pleocytosis defined as: CSF WCC of  $\geq 19$  white cells per  $\text{cm}^3$   $\leq 28$  day group;  $\geq 9$  WCC/ $\text{cm}^3$  in the 29 days to 11 months group; and  $\geq 5$  WCC/ $\text{cm}^3$  for children  $\geq 12$  months.
- A low CSF [glucose] was defined as one which was less than two thirds of the blood [glucose] taken within two hours of the CSF.

**Confirmed Enterovirus Meningitis:** Enterovirus detected in CSF\*, and/or throat, rectal or stool samples by real-time PCR/culture.

**Probable Enterovirus Meningitis:** Clinical criteria **plus** detection of enterovirus in a throat and/or stool sample when no other pathogen was identified.

**Clinical criteria confirmed case of Enterovirus Meningitis:** fever, meningism, and/ or irritability in neonatal cases.\*

\*Fever and/ or an elevated cerebro-spinal fluid (CSF) white cell count (WCC) were not absolute requirements in those cases where enterovirus was detected in (CSF).

Table 1: Meningitis Definitions Used in the Study

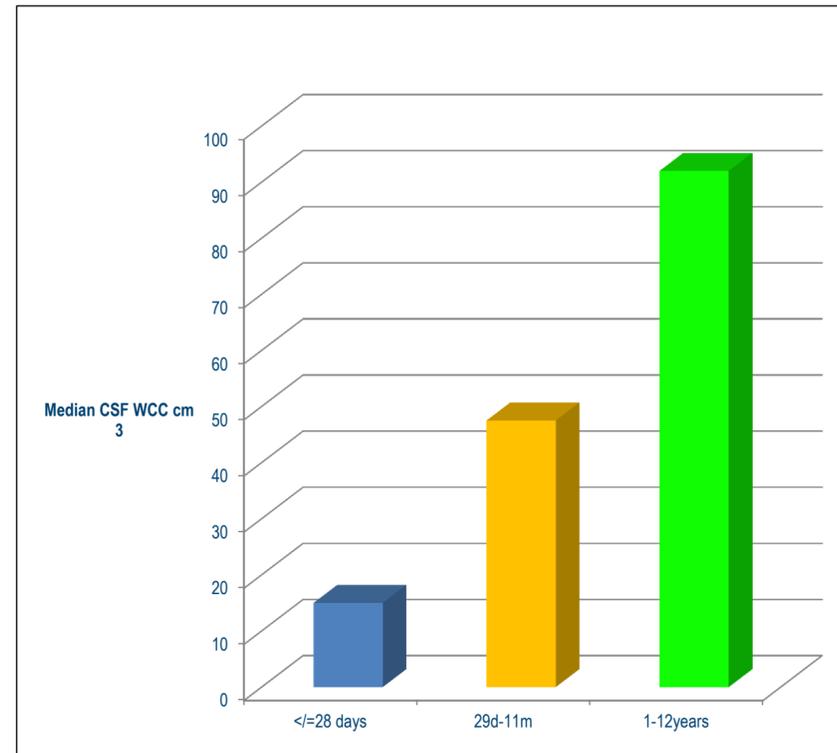


Figure 1. Median CSF white cell counts in patients with enterovirus meningitis according to age group

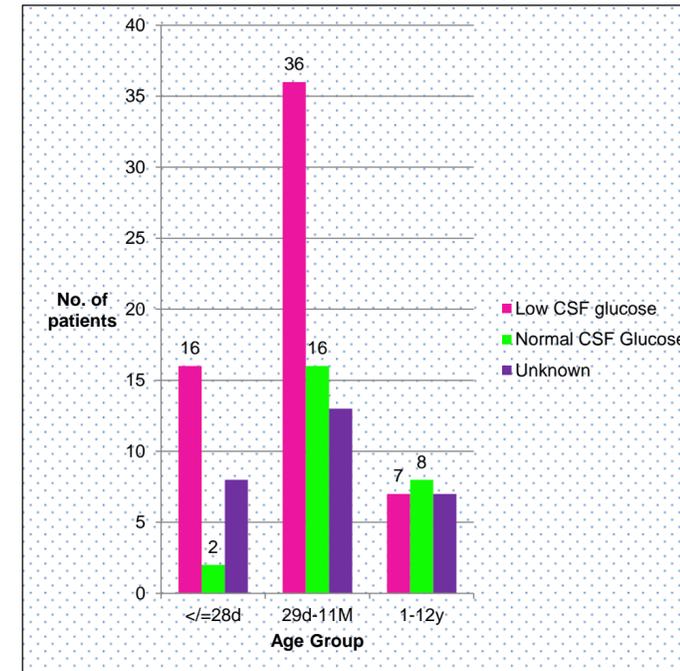


Figure 3. Features of CSF glucose concentration in enterovirus meningitis according to age group

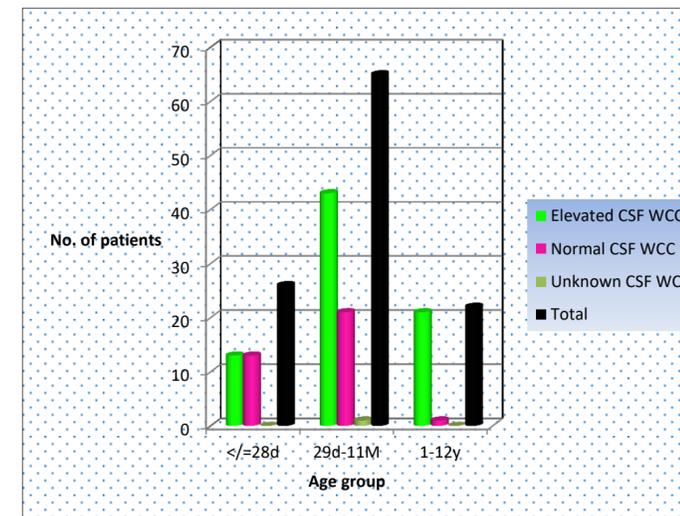


Figure 2. CSF white cell count levels in patients with enterovirus meningitis according to age group

## Results

- 113 cases of enterovirus meningitis were reviewed, age range 0.1 months to twelve years: 84 per cent of cases (95/113) met the confirmed case criteria.
- Twenty-six cases were identified in the  $\leq 28$  day age group, sixty-five in the 29 day to 11 month group, and 22 in the 1-12 year group.
- The average age was 1.73 months in the non-pleocytosis group and 22.4 months in the pleocytosis group (median age 1.6 months overall).
- The average overall CSF WCC was 149 per  $\text{cm}^3$  (range: 0-1160).
- The median age, and CSF white cell count was 1 month, and  $2/\text{cm}^3$  in the non-pleocytosis group, and 2 months and  $93/\text{cm}^3$  in the pleocytosis group, respectively.
- Patients in the non- pleocytosis groups were found to be significantly younger than those in the pleocytosis group ( $P < 0.001$ )\*\*.
- A low CSF glucose concentration was observed in 52% of patients (59/113). \*\*Mann-Whitney test.
- Eighteen, eleven and sixteen per cent of neonates, 29 day – 11 month and 1- 12 year olds were afebrile on examination, respectively.

## Conclusions

- A normal CSF white cell count and a low CSF glucose concentration were found to be features of enterovirus meningitis in this study. These factors were particularly evident in children under one year. Of note, fever was absent in up to 18% of these children.
- We conclude that enterovirus meningitis should still be a consideration in infants with a normal CSF white cell count.
- Consideration should also be given to broadening the criteria for clinical and laboratory case definitions for viral meningitis. This would facilitate hospital discharges, the discontinuation of antibiotics and an understanding of the true burden of this common childhood infection.