Short reports

Cerebrospinal fluid immunoglobulins in children

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SUMMARY Cerebrospinal fluid (CSF) immunoglobulins were measured in 62 normal children, in 9 children with purulent meningitis, and in 10 children with presumptive viral meningitis. The mean values in normal children were IgA 0, IgM 0, and IgG 0.84 ± 1.4 mg/100 ml ($\pm$ SD). The mean levels of all CSF immunoglobulins were raised in acute bacterial meningitis and were significantly greater than the levels found in viral meningitis. CSF IgM was 0.16 ± 0.5 mg/100 ml in viral meningitis compared with 2.64 ± 2.06 mg/100 ml in bacterial meningitis ($P < 0.01$). However, these values overlapped to a considerable extent and, generally, measurement of CSF immunoglobulins did not enhance diagnostic accuracy in this group of children.

Smith *et al.* (1973) presented data on CSF immunoglobulins in meningitis in adults, and suggested that the levels of IgM might help to distinguish viral from bacterial meningitis.

Methods and material

CSF immunoglobulins were measured in 81 children aged between 0.1 and 10½ years. The indications for spinal tap were meningitis, suspected meningitis, convulsions, or (for therapeutic purposes) leukaemia. The 62 children designated as normal had WBC $< 10 \times 10^6/l$ ($< 5 \times 10^6/l$ in all except 4), and normal CSF protein and glucose relative to age. Most of the children were being evaluated for suspected meningitis or because they had had febrile convulsions. Nine children were considered to have bacterial meningitis, of which 3 proved to be due to *Haemophilus influenzae*, 3 to *Neisseria meningitidis*, 1 to *Staphylococcus albus*, and 2 showed no growth on culture. In 10 children meningitis was presumed to be viral in origin on the basis of leucocyte response, CSF protein and glucose levels, and clinical course. Specific viral cultures were not performed.

Lumbar puncture was performed as indicated on admission and the CSF analysed routinely in the laboratory. An unspun aliquot of the CSF was stored at 4°C before the immunoglobulins were estimated. CSF immunoglobulins were measured without knowledge of the child's clinical or routine CSF findings. Cerebrospinal fluid samples which were grossly blood-stained or which contained RBC $> 100 \times 10^6/l$ were discarded.

CSF immunoglobulin concentrations were measured by the radial immunodiffusion method (Mancini *et al.*, 1965), using commercial L.C. Partigen plates and pooled human serum (Behring) as standard. 5 µl centrifuged, undiluted CSF was placed in the application wells and incubated for 72 hours at room temperature. Appropriate dilutions of standard in normal saline were also prepared. To intensify the precipitin ring the IgM and IgA plates were rinsed in phosphate-buffered saline for 24 hours, then covered with a 4% aqueous solution of tannin for 30 minutes and washed with distilled water. Standard curves were prepared from the square of the precipitin rings.

Results

Table 1 shows that IgA and IgM were not detected in

Table 1 Clinical and CSF findings in 81 children (mean $\pm$ SD)

	Normal CSF (n = 62)	Viral meningitis (n = 10)	Bacterial meningitis (n = 9)
Mean age (years)	2.4	5.1	1.5
(Range)	(0.1-10.0)	(0.7-10.5)	(0.3-4.5)
WBC ($\times 10^6/l$)	1.95 ± 2.0	148.1 ± 91.5	2352.1 ± 2756.0
Polymorphs (%)	—	43.4 ± 29.3	70.6 ± 29.9
Lymphocytes (%)	—	56.6 ± 21.6	29.4 ± 32.4
Protein (mg/100ml)	12.9 ± 9.6	31.0 ± 28.5	163 ± 120.3
Glucose (mg/100 ml)	59.7 ± 16.7	63.8 ± 15.4	15.1 ± 16.3
IgA mg/100 ml	0.0	0.0	1.89 ± 2.2
IgM mg/100 ml	0.0	0.16 ± 0.5	2.64 ± 2.06
IgG mg/100 ml	0.84 ± 1.4	4.19 ± 9.1	17.88 ± 6.21

Conversion: traditional units to SI—CSF proteins: 1 mg/100 ml $\approx$ 0.01 g/l, glucose: 1 mg/100 ml $\approx$ 0.0555 mmol/l.

the CSF of normal children, 69% of whom were aged under 3 years; IgG ranged from 0.1 to 3.6 mg/100 ml with a mean IgG level of 0.84 mg/100 ml. In the 10 children with viral meningitis, IgM was undetectable in 9 children and present in a concentration of 1.6 mg/100 ml in one child; IgM was undetectable in 2 children with bacterial meningitis, and in the remainder it ranged from 0.75 to 5.1 mg/100 ml (mean 2.64). IgG levels were raised in excess of 5 mg/100 ml in 7 of 9 children with bacterial meningitis. The mean levels of all CSF immunoglobulins, particularly IgG, were significantly higher in bacterial than in viral meningitis (Table 2).

Discussion

It is known that serum immunoglobulins are lower in children than in adults. At age 1–2 years serum IgG, IgM, and IgA are 66, 59, and 25% of respective adult values (Stiehm and Fudenberg, 1966). It is believed that CSF immunoglobulins are derived by

Table 2 Significance in the differences (mean $\pm$ SD) in distribution of CSF substances in three groups of children using the Mann-Whitney U test

CSF	Normal v. viral	Normal v. bacterial	Viral v. bacterial
Protein	P<0.01	P<0.01	P<0.01
Glucose	NS	P<0.01	P<0.01
IgA	NS	P<0.01	P<0.05
IgM	NS	P<0.01	P<0.01
IgG	P<0.05	P<0.01	P<0.05

diffusion from serum, although the lymphoid tissue may produce IgG (Lord *et al.*, 1973).

In the present study a statistically significant difference in CSF IgG levels was shown between normal children and those with viral or bacterial meningitis, although the levels overlapped. High levels of CSF IgG (>5 mg/100 ml) were found in 7 children, and high levels of IgM (>3 mg/100 ml) in 5 of 9 children with bacterial meningitis.

Retrospectively, CSF immunoglobulins did not enhance the diagnostic accuracy of acute childhood meningitis as similar information could be gained from study of the total differential white cell count in combination with protein and glucose analyses (Table 1).

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Treatment of a neonate with propionic acidaemia and severe hyperammonaemia by peritoneal dialysis

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SUMMARY A moribund newborn infant with propionic acidaemia and severe hyperammonaemia was successfully treated by peritoneal dialysis. The removal of ammonia and possibly additional toxic metabolites by peritoneal dialysis may be life-saving in newborn infants with propionic acidaemia or other hyperammonaemic syndromes.

Propionic acidaemia is a rare inborn error of metabolism which can be present in the neonatal period with persistent ketoacidosis and altered neurological status (Rosenberg, 1978). Survival of an

infant thus affected depends on rapid diagnosis and immediate institution of measures to alleviate the chemical imbalances accompanying the disease. The usual treatment is to restrict the proteins while maintaining adequate calories and fluids to prevent the accumulation of harmful metabolites, but occasionally deterioration of the condition of the patient necessitates more drastic removal of these metabolites. We report a case of a neonate with propionic acidaemia who had extremely high blood ammonia concentrations with coma, but who survived after the rapid removal of ammonia by peritoneal dialysis.