Echovirus 19 infection in infants under six months

C. J. BACON and D. G. SIMS

From the Departments of Child Health and Virology, Royal Victoria Infirmary, Newcastle-upon-Tyne

Bacon, C. J., and Sims, D. G. (1976). *Archives of Disease in Childhood*, **51**, 631. **Echovirus 19 infection in infants under six months.** Twenty-four infants under 6 months infected with echovirus 19 are described. They were the youngest of the many children admitted to hospitals in Newcastle and Gateshead during an epidemic in the north-east of England in 1974. Generally, the younger the child the more severe the illness, which affected the upper respiratory tract, the gut, the skin, and the meninges, and sometimes caused a state of collapse resembling septicaemic shock. Polymorphonuclear pleocytosis of the cerebrospinal fluid (CSF) sometimes suggested bacterial meningitis, so that antibiotics were given in 38% of cases. The virus was recovered with a high success rate from nasopharyngeal secretions, CSF, and stool.

During the summer of 1974 there occurred in the north-east of England an epidemic of echovirus 19 far larger than any previously recorded, 267 cases being identified, the majority in children (Codd *et al.*, 1976). In older children the illness took well-recognized forms, such as aseptic meningitis, abdominal pain, inflammation of the upper respiratory tract, and febrile convulsions, but in babies manifestations were more varied and severe, and sometimes hard to distinguish from bacterial infection. 24 infants aged 6 months and under are described who were admitted to hospitals in Newcastle and Gateshead.

Clinical and laboratory findings

The 24 cases occurred at all stages of the epidemic. 21 were admitted with the infection and 3 developed it soon after admission for unrelated conditions. The main clinical features are given in the Fig. The illness began with irritability, drowsiness, and reluctance to feed. All but the mildest cases then developed disturbances of the respiratory tract, the gut, the meninges, or the skin. All were febrile, with a maximum temperature of about 39.5°C, though 41°C was recorded on one occasion. The illness lasted from 3 to 16 days and was generally more severe in younger babies. All but one case made a full recovery.

Respiratory involvement consisted of nonexudative pharyngitis, otitis media, sometimes coryza but not usually a cough. The only lower respiratory manifestation was bronchospasm, which occurred in 2 babies who had had previous attacks of wheezing. Vomiting and

diarrhoea often occurred, and sometimes screaming attacks suggestive of intestinal colic. The abdomen was normal on palpation. Lymph nodes were not enlarged. 10 babies developed a punctate erythematous macular or maculopapular rash on the second or third day of the illness. It was most marked over the face, neck, and upper trunk sometimes coalesced to become confluent, and faded after about 5 days. There were no oral lesions. Occasionally the eyelids were puffy.

Four of the smaller babies (aged 3, 4, 6, and 11 weeks) deteriorated rapidly into a state of collapse with peripheral circulatory failure and cyanosis. In the pre-

FIG.—Main clinical features of 24 cases.

Received 19 November 1975.

TABLE I
Findings in 22 specimens

Day	2	2	3	2	4r	2	4	3	10r	10
WBC (mm ³)	99	5	17	390	470	4	270	>1000	28	21
Polymorphs (%)	38	—	55	96	96	—	15	95	100	65
Protein (mg/100 ml)	33	22	—	70	—	74	100	91	73	100
Viral culture	+	+	0	+	—	+	—	+	+	—

Day, day after onset of illness that CSF was examined; r, repeat lumbar puncture in same case.

sence of fever and a rash their condition was clinically indistinguishable from bacterial septicaemia, and as soon as specimens had been taken they were treated with systemic antibiotics and intravenous fluids including plasma. Pleocytosis of the cerebrospinal fluid (CSF) in 2 of them suggested bacterial meningitis as well.

Meningitis was often suspected because of fever, irritability, and drowsiness, and increased tension of the anterior fontanelle in 3 infants. 13 of the 16 babies who had lumbar punctures proved to have meningitis, as defined by the presence of $>10/\text{mm}^3$ white cells in the CSF or a positive viral culture. There were 2 possible cases of encephalitis: one infant aged 6 weeks but born 2 months preterm had apnoeic attacks, while another aged 11 weeks had several convulsions; an electroencephalogram of the latter was normal. One infant with an endocardial cushion defect and heart failure developed echovirus 19 meningitis 2 days before death.

The peripheral blood of 16 babies was examined and the white cells were unremarkable the totals ranging from $5200\text{--}17\,000/\text{mm}^3$ (mean $11\,750$) and the proportion of lymphocytes, all of normal morphology, from 10%–77% (mean 54%). In 22 specimens of CSF examined (Table I) glucose was always normal but protein was sometimes raised as high as 100 mg/100 ml. Pleocytosis was often marked, on one occasion enough to make the fluid cloudy, and polymorphs predominated in two-thirds of the specimens. Suspicious CSF findings prompted treatment with antibiotics in 5 babies, and in 4 continuing concern about bacterial infection resulted in a second or third lumbar puncture.

Viral studies were performed by the Department of Virology of Newcastle University or by the Public Health Laboratory as described by Codd *et al.* (1976). The presence of an enterovirus was reported in 2 to 6 days and it was typed in a further 2 days. The site of isolation of the virus (Table II) did not always correlate with clinical findings. For example, the virus was always recovered from stool whether or not there was diarrhoea, and often from nasopharyngeal secretions when no pharyngitis was apparent, and sometimes from CSF which contained no excess of white cells. Bacterial stains and cultures were performed as appropriate and no concomitant infections were found. Chest x-rays were normal, except of the infant with heart disease.

TABLE II

Results of all attempts at viral culture from 24 cases

Specimen	Culture attempted	Virus isolated
Nose swab, throat swab	19	13
Nasopharyngeal secretions	19	15
CSF	14	11
Stool	8	8

Discussion

It appears that the earlier in life infection occurs the more serious the illness. In neonates it may be fatal, and 3 deaths have been reported (Philip and Larson, 1973), the infection in one case probably being congenital. Fatal pulmonary emphysema in a preterm infant has been associated with echovirus 19 infection (Butterfield *et al.*, 1963), but the evidence that the virus caused the illness was not strong. In our patients the most striking presentation was that resembling bacterial septicaemia. Although vomiting and diarrhoea had not been sufficient to cause much dehydration, there appeared to be hypovolaemia such as occurs in babies with serious bacterial infection (Aynsley-Green and Pickering, 1974), and the condition might by analogy be called 'viraemic shock'.

It was sometimes difficult to distinguish viral from bacterial meningitis. CSF cell counts of up to 1000 polymorphs/mm³ suggested bacterial infection, and when antibiotics had been given before admission the failure to show bacteria by direct stain or on culture was not exclusive. A polymorph pleocytosis is not unusual in early aseptic meningitis, but in 4 of our cases where lumbar puncture was repeated there was no change to a lymphocytosis later. The recovery of virus from CSF of normal cellularity suggests that viral culture of CSF is valuable regardless of cell count.

I

of CSF from 16 cases

3	5	2	2	2	4	5r	2	3r	10r	2	3
4	8	1	2	17	60	0	0	43	26	—	13
—	—	—	—	30	80	—	—	56	—	—	75
25	60	20	26	10	23	—	15	16	12	59	24
+	0	0	+	—	+	+	+	—	+	—	+

+, virus grown; 0, no virus grown; —, investigation not performed or results not available.

Thus 9 of our babies (38%) were treated with antibiotics because of the possibility of bacterial septicaemia or meningitis. The necessity of this precaution in doubtful cases was illustrated by another baby which presented in the midst of the epidemic with an illness identical with echovirus infection, including typical CSF findings, and was not at first given antibiotics, but 10 hours later developed meningococcal purpura and did not respond to the treatment then instituted.

Viral identification by culture comes too late to determine initial management, but may save some babies from further antibiotics and shorten their stay in hospital. The possible development of rapid viral diagnosis by immunofluorescence offers the prospect that, in a future echovirus 19 outbreak, identification can be made within a few hours of admission (P. S. Gardner and J. McQuillin, personal communication).

We thank the paediatricians who allowed us to report their cases; the pathologists who identified the virus and advised in the preparation of this paper (in particular Professor P. S. Gardner, Dr. A. A. Codd, and Dr. T. M. Bell); and the Medical Research Council whose grant finances one of us (D.G.S.).

REFERENCES

- Aynsley-Green, A., and Pickering, D. (1974). Use of central and peripheral temperature measurements in care of the critically ill child. *Archives of Disease in Childhood*, **49**, 477.
- Butterfield, J., Moscovici, C., Berry, C., and Kempe, C. H. (1963). Cystic emphysema in premature infants. *New England Journal of Medicine*, **268**, 18.
- Codd, A. A., Hale, J. H., Bell, T. M., Sims, D. G., Bacon, C. J., and Gardner, P. S. (1976). Epidemic of echovirus 19 in the north-east of England. *Journal of Hygiene*, **76**, 307.
- Philip, A. G. S., and Larson, E. J. (1973). Overwhelming neonatal infection with echo 19 virus. *Journal of Pediatrics*, **82**, 391.

Correspondence to Dr. C. J. Bacon, Dept. of Child Health, Royal Victoria Infirmary, Newcastle-upon-Tyne NE1 2QU.