Antibiotic treatment of suspected neonatal meningitis

Sir,—The editorial by Drs Gandy and Rennie on antibiotic treatment of suspected neonatal meningitis has provided a timely review of an important neonatal problem. We were surprised to see the use of intraventricular aminoglycosides being advocated for the treatment of Gram negative meningitis, as there is now considerable evidence to suggest that intraventricular treatment is not only ineffective, but may, in addition, be hazardous. We were further disappointed to read the authors' rebuttal of the important arguments made by Drs Short and Taylor in their subsequent letter to the editor.

The argument put forward by Gandy and Rennie rests on the observation that the aminoglycosides do not penetrate well into the cerebrospinal fluid, and that cerebrospinal fluid concentrations of Gram negative bacillary meningitis are not achieved when aminoglycosides are administered intravenously. In the past, intrathecal aminoglycosides seemed a logical form of treatment. Since the introduction of the third generation cephalosporins, however, the position has changed. These agents are highly active against Escherichia coli and other coliforms, and when administered intrathecally, achieved cerebrospinal fluid concentrations several times the minimal inhibitory concentration for these organisms. Therefore, the use of intraventricular treatment is not considered beneficial by us.

The authors seem unconvinced by two multicentre trials of intrathecal aminoglycosides in neonatal meningitis. Not only was there no benefit derived from aminoglycosides given by either the lumbar or the intraventricular route, but the mortality was higher in the patients receiving intraventricular treatment. The authors also avoid the worrying evidence that suggests that the administration of intraventricular aminoglycosides results in higher cerebrospinal fluid concentrations of endotoxin and cytokines than seen after systemic treatment alone. In view of the increasing evidence that bacterial toxins and host inflammatory mediators are responsible for the damage to the central nervous system associated with bacterial meningitis, treatment that increases cerebrospinal fluid concentrations of these substances should be avoided.

The authors have developed subsequent to the annotation on the antibiotic treatment of suspected neonatal meningitis a different approach to what makes good paediatric practice. We believe that practice should be guided by the results of published therapeutic trials rather than theoretical considerations. The only trials that have demonstrated a poorer outcome in patients receiving intraventricular aminoglycosides, a form of treatment that should not be advocated.

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4 Kaplan SL. Recent advances in bacterial meningitis. Advances in Pediatric Infectious Diseases 1989;4:63-81.
5 McCracken GH, Mize SG, Threlkeld N. Intraventricular gentamicin therapy in gram negative bacillary meningitis of infancy. Lancet 1980;i:787-91.

Drs Gandy and Rennie comment:
The correspondence generated by our editorial has highlighted the difficulties experienced by those attempting to manage this condition. We endorse the use of cefotaxime but, as stated in the original annotation, the published results have shown that it contains only small numbers of babies (less than 50) and there has not been the improvement in mortality or morbidity which was expected. This could be because of the use of intraventricular enlargement in neonatal cases which may require drainage or make the cerebrospinal fluid minimal inhibitory concentration inadequate, and it is for these babies and for those who fail to respond to systemic therapy alone that we continue to recommend consideration of intraventricular treatment. The use of intraventricular reservoirs will naturally decline if it is possible to have the success which is predicted for them.

Drs Heyderman and Levin are correct in their assumption that we remain unconvinced by results regarding 20 neonates with Escherichia coli meningitis contained in the only study using intraventricular treatment which was carried out before the introduction of cephalosporins, ultrasound, or intraventricular reservoirs. We agree that clinical practice should be guided by the results of well conducted therapeutic trials of adequate size but for neonatal Gram negative meningitis we consider that such studies are yet to be published, and urgently need to be planned.

1 McCracken GH, Mize SG, Threlkeld N. Intraventricular gentamicin therapy in gram negative bacillary meningitis of infancy. Lancet 1980;i:787-91.

Categories of preventable unexpected infant deaths

Sir,—As members of the Avon Infant Mortality Study Group we were surprised and disturbed by the recent paper from Sheffield by Taylor and Emery. They came to the conclusion that in 43% of sudden unexpected infant deaths there was 'treatable disease' and, by implication, these deaths could have been prevented by appropriate health care intervention. This finding is in variance with our own observations. We were also concerned to read that eight of 115 (7%) deaths in the Sheffield study were attributed to filicide, a finding which is at variance with our own experience of only one case of proved filicide in over 200 sudden unexpected death victims during a seven year period in Avon.

We see the parents of all infants who die unexpectedly in Avon within 72 hours of the death (most of them within 24) with the general practitioner and health visitor and collect detailed information from the parents, primary care team, and hospitals. This contact includes a 'death scene' examination and a structured questionnaire on medical and social history. All infants had a detailed standardized postmortem examination by a paediatric pathologist or a pathologist with special expertise in this field.

For the past three years all sudden unexpected deaths of infants in Avon have been the subject of a formal multidisciplinary confidential discussion involving two pathologists, a microbiologist, a biochemist, an epidemiologist, and three paediatricians with extensive experience of infant care.

We have drawn up a classification of death using microbiological, gross pathological, and histological criteria. The results of the 95 infant deaths included in the first two years of our study (May 1987 to April 1989) are given below.

In seven (8%) of the total deaths we were able to identify a sufficient causative factor, which, in 39 (41%) we identified evidence of a potentially significant illness at the time of death, but insufficient to account for the death. In the remaining 49 (51%) no significant abnormalities were identified. Many of these deaths was thought to be due to filicide. These results are similar to those previously published by Arneil et al in the Scottish National Study.

Taylor and Emery state that minor non-lethal defects may lower the threshold for the onset of severe illness and thus contribute to death. We are not aware of any evidence to support this contention. Such thresholds are very low and our experience is very common, and interpretation of their significance as contributory factors in infants who die requires carefully matched controls, which are lacking in the Sheffield study.

Workers in the field of sudden unexpected death in infancy have a great responsibility to the children of this country and to the parents of children who have died suddenly of illness unexpectedly. The paper by Taylor and Emery raises many questions about the interpretation of clinical, psychosocial, and pathological factors after the death. They contain insufficient data to allow the reader to assess the validity of their conclusions.

We are well aware of the confidential nature of inquiries that have to be made where filicide is considered to be a possibility, but we call upon the authors of this work to make available the information that they have for confidential re-examination by an independent group of paediatricians and pathologists. The outcome of this fresh inquiry could then be submitted for publication in this journal.

These questions are too important to be left open by the lack of data in the paper by Taylor and Emery.

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