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.1 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 Short2 and Tarlow3 in their subsequent letter.4

The argument put forward by Gandy and Rennie rests on the observation that the aminoglycosides do not penetrate well into the cerebrospinal fluid, and adequate cerebrospinal fluid concentrations to treat 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 intraventricularly, achieved cerebrospinal fluid concentrations several times the minimal inhibitory concentration for these organisms.4 It is therefore difficult to justify the use of intraventricular treatment.

The authors seem unconvinced by two multicentre trials of intrathecal aminoglycosides in neonatal meningitis.5 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.5 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,6 treatment that increases cerebrospinal fluid concentrations of these substances should be avoided.

The arguments that have developed subsequent to the annotation on the antibiotic treatment of suspected neonatal meningitis highlight the different philosophical approaches to what makes good paediatric practice. We believe that practice should be guided by the results of published therapeutic trials rather than the authors' personal belief. We are concerned that the only trial of intraventricular aminoglycoside therapy has demonstrated a poorer outcome in patients receiving intraventricular aminoglycosides, this form of treatment should not be advocated.

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4 Kaplan SL. Recent advances in bacterial meningitis. Advances in Pediatric Infectious Diseases 1999;4:63-110.

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 do not contain one for 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 lack of variability in the treatment of meningitis or lack of proper follow-up of patients.

We have found that the treatment of suspected meningitis has provided a timely review and a rebuttal of the important arguments made by Drs Short and Tarlow, which was an important 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 cause, which, in 39 (41%) we identified evidence of a potentially significant illness at the time of death, but insufficiently to account for the death. In the remaining 49 (51%) no significant abnormalities were identified. Some of these deaths was thought to be due to infection. These results are similar to those previously published by Arneil et al in the Scottish National Study.8

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. Studies of deaths of neonates are very common,9 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 in infancy. The paper by Taylor and Emery raises many questions about the interpretation of clinical, psychosocial, and pathological factors after the death of an infant. It contains 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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Effective bronchodilator treatment by a simple spacer device for wheezy premature infants

SIR,—Yuksel and colleagues describe a cheap and easy solution to a common and difficult problem. 1 It cannot help but be impressed by the size of the improvement seen during active treatment.

There are, however, certain aspects of the study which concern me. Firstly, the study was not randomised and all the children were given active treatment after placebo. Although this is disputed by the authors, in this group of children where symptoms are likely to have been exacerbated by viral infections, one would have expected some improvement with time, irrespective of treatment. This possibility is borne out to some extent, as on active treatment there was a 27% reduction in the score for 'runny nose/unwell'; these are symptoms which are suggestive of a viral infection. These symptoms could not have been expected to respond to a bronchodilator and therefore should not have been added to cough and wheeze (their table 1). Also adding together scores for cough and wheeze (their table 1) could double the score for a single event. Admittedly the percentage fall in each symptom category, with active treatment, is remarkable.

Secondly, the authors state 'Administration of the bronchodilator resulted in an increase in functional residual capacity both immediately after treatment and during the two week active period'. This is patently not borne out by the results in their table 3, where there is no significant difference in functional residual capacity before and after terbutaline (mean 275 (SD) 269 (58) in the placebo period and 322 (83) and 325 (95) in the active period). Indeed two and three subjects, respectively, showed a 'clinically significant' decrease in functional residual capacity after terbutaline compared with four and two with a 'clinically significant' increase. If we are to believe, as the authors suggest, that an increase in functional residual capacity reflects an improvement in lung function, then the long term improvement in functional residual capacity on active treatment occurred without any evidence of an immediate response. The authors do not address this discrepancy between the long and the short term benefit but misleadingly suggest that an immediate benefit of the functional residual capacity had occurred.

One is left with a sneaking suspicion that at least part of the improvement on active treatment, in symptoms and lung function, could be related to changes with time. Before accepting the alternative conclusion, that in this group of children twice daily terbutaline has a dramatic effect on symptoms, which is largely independent of its immediate bronchodilator properties, it would be wise to confirm the results with a better designed study.


Dr Greenough and Yuksel comment:

We thank Dr Wilson for her interest in our paper. In that preliminary study, as no previous data was available, we set out to assess if bronchodilator given by a simple spacer had any effect on symptomatic preterm infants in the first year of life. We found over the two week period in which bronchodilator was administered a significant improvement in lung function and reduction in symptom score.

We are surprised Dr Wilson felt it necessary to reanalyse the acute lung function data as we did not claim that the change in functional residual capacity for 10 minutes after treatment was significant. We recognised and stressed in our discussion that the results could in part be explained by an improvement in symptoms with time and felt our results should be confirmed in a randomised trial—which, as a consequence we have subsequently completed (unpublished observations). In a randomised placebo controlled trial inhaled ipratropium bromide administered via a coffee cup, resulted in similar improvements in functional residual capacity and a reduction in symptom score. Unfortunately many infants are symptomatic in the first year of life, the coffee cup technique is cheap and easy; we therefore, like Dr Wilson, are impressed and we are also pleased with the size of improvement seen during active treatment. 1