Antibiotic treatment of suspected neonatal meningitis

Sir,—The annotation on antibiotic treatment of suspected neonatal meningitis seems to demonstrate that optimal treatment of this thankfully rare disorder is still not clear. The suggested array of antibiotic treatment and combined routes of administration may provide cover against a wide range of organisms, but is such treatment in the best interests of every patient? In a sick hypotensive infant who may already have compromised renal function the combination of aminoglycoside and cephalosporin may exacerbate the problem. To state that ‘Gentamicin should be used primarily to treat the associated septicaemia’ misses the point that the inclusion of cephalosporins is incapable of doing this. Is there any evidence to suggest that cefotaxime is ineffective in the treatment of bacteremia in neonates? I am concerned by the conviction of the authors in their management proposals. To begin a paragraph stating ‘there is no doubt in our minds that intraventricular treatment should be used’ and end it with ‘there has been no study of intraventricular treatment...’ and little information on the intraventricular drug concentration achieved after systemic treatment alone in dilated ventricles’ is perhaps a little rash in view of the findings of significantly increased mortality after intraventricular treatment in the American study.

The conclusion of McCracken and colleagues was that ‘intraventricular therapy cannot be recommended for the routine management of neonatal meningitis caused by Gram negative enteric bacilli’. In the absence of a further randomised multicentre trial it is surely ill advised to recommend the adoption of this invasive and potentially dangerous mode of treatment as the standard treatment in neonatal Gram negative meningitis with ventricular dilatation.


Sir,—The main thrust of the annotation on antibiotic treatment of neonatal meningitis is the recommendation that antibiotics should be used intraventricularly as well as intravenously, particularly in the babies infected with Gram negative enteric organisms. The authors mention the only significant study in the field, that of McCracken et al (1980),2 only to dismiss its findings (there was a higher mortality in the group treated with intraventricular therapy) on the grounds that many of the infants had salmonella infection and were treated relatively late. This interpretation does not take into account the advanced stage in our understanding of the pathophysiology of meningitis, and is likely to lead to a simplistic approach to clinical management. It is now known that the inflammatory response in meningitis (and in many other infective conditions) is mediated through the release of cytokines, particularly tumour necrosis factor and interleukin-1, from cells after their exposure to bacterial endotoxin and other cell wall material. Interleukin-1 concentrations in the cerebrospinal fluid correlate well with the degree of meningeal inflammation and with the outcome. Ventricular cerebrospinal fluid samples from the 1970s study performed by McCracken and his colleagues were stored in the deep freeze at the time, and their endotoxin and cytokine concentrations have recently been examined by Mustafa et al (1989).3 They found increased endotoxin and very much higher interleukin-1 concentrations in the cerebrospinal fluid of the group treated with intraventricular antibiotics than in those only treated intravenously. Endotoxin concentrations of 78 ng/ml in the intraventricular group compared with 22 ng/ml in those given intravenous treatment alone. Similarly, mean interleukin-1 concentrations as high as 5024 pg/ml in the patients given gentamicin with葛ram-negative bacilli contrasted with mean concentrations of 87 pg/ml in patients treated with intravenous antibiotics alone. This effect is likely to be due to bacterial lysis releasing endotoxin and other bacterial cell wall products with very high local concentrations of intraventricular gentamicin. The resulting cytokine production would appreciably exacerbate the inflammatory response within the ventricles. Thus although intraventricular antibiotics may be appropriate treatment in neonatal meningitis (although there is little firm evidence otherwise), it is important to modulate the resultant inflammatory response as well as to kill the bacteria. Considerable recent work, particularly from McCracken’s group, has shown that dexamethasone can do this both in the experimental animal model and in children with Gram-negative meningitis.4 Until we recognise that the treatment of meningitis should include the suppression of excessive inflammation as well as the destruction of the pathogen we are unlikely to improve the prognosis in this serious and distressing disease.


When should the coeliac patient have an intestinal biopsy?

Sir,—Gluten challenges and intestinal biopsies are stressful procedures both for coeliac patients and for the doctors dealing with them. While we recognise that the time has...