

LETTERS TO THE EDITOR

Prospective surveillance of neonatal meningitis

EDITOR,—We read the paper by Hristeva *et al* on neonatal meningitis with interest.¹ Their study included only those infants on a neonatal unit. A previous study has shown that 45% of neonatal meningitis is seen in infants admitted from home² and this population would not be represented in the study of Hristeva *et al*. Their incidence of bacterial meningitis at 0.25/1000 live births could therefore be an underestimate.

A review of neonatal meningitis in Liverpool between 1984 and 1988 revealed 34 cases: 20 treated in neonatal units and 14 in the wards of the local children's hospitals. The incidence of bacterial meningitis in infants born to mothers resident in Liverpool and South Sefton health districts was 0.33/1000 live births (that is 16 out of 48 369 deliveries; HM Thomas, unpublished data). This is similar to the figure of de Louvois and Harvey of 0.32/1000.² Dr Hristeva *et al* state that none of the 11 infants who completed treatment for bacterial meningitis relapsed. In Liverpool over a 10 year period two cases of neonatal meningitis have relapsed after discharge, both due to *Escherichia coli*. Both were admitted to a children's hospital for treatment of the second episode and would also have been missed by the study of Dr Hristeva *et al*.

Finally, Dr Hristeva *et al* conclude that lumbar puncture may be deferred in the first 48 hours after birth and need only be performed if blood cultures are positive. This is not supported by their own data as in two of the eight early cases blood cultures were negative and antibiotic treatment was directed by the results of lumbar puncture in these cases. In two other recent studies blood cultures were negative in 18 out of 35 infants with bacterial meningitis on the first two days of life.^{3,4} We agree that a lumbar puncture should be deferred in any infant in a poor clinical condition. But we believe that a lumbar puncture should be performed if meningitis is clinically suspected and should not be avoided solely on the basis of negative blood cultures.

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Drs Booy, Bowler, and Wilkinson comment:

We recognised in our paper that the true incidence of neonatal meningitis was likely to be higher than we had calculated as we stated

that we had not included neonates who developed meningitis after discharge. Dr Thomas and colleagues have misunderstood our paper with respect to whether lumbar puncture should be performed in the first 48 hours after birth. We gave the caveat that *when the clinical condition is poor* it is reasonable to defer. They agree with this approach. If a newborn is fit for lumbar puncture and meningitis is suspected, then lumbar puncture should be performed. If unfit, for example because of cardiorespiratory compromise, the lumbar puncture should be delayed but still performed later when the child can tolerate the procedure.

Randomised trial of methods of extubation in acute and chronic respiratory distress

EDITOR,—The paper of Chan and Greenough, which assesses the effect of nasal continuous positive airway pressure (CPAP) after endotracheal extubation,¹ is a good example of how a non-significant result from a small study can be potentially misleading. From a study of two groups of 60 infants the authors concluded that there was no significant difference in the failure rate of extubation among infants randomised to receive either nasal CPAP or headbox oxygen in both acute or chronic respiratory distress groups. They concluded that the decision to use nasal CPAP after extubation should be individualised, perhaps using atelectasis after extubation as a criterion.¹

However, when one looks more closely at the results of extubation in the acute respiratory distress group it can be seen that eight of 30 babies randomised to nasal CPAP failed compared with 13 of 30 babies allocated to headbox oxygen. The difference in these proportions suggests a 17% lower failure rate in the babies treated with nasal CPAP indicating that one in six infants with acute respiratory distress may benefit from the use of nasal CPAP as opposed to headbox oxygen. However, the 95% confidence interval for the difference in percentages² is from -7% to 40% showing that these results are also consistent with as many as two in five infants benefiting from nasal CPAP. The authors had used the results of a retrospective review to calculate a trial size for this prospective study. Sixteen (32%) of 50 infants in the retrospective review had failed extubation (a 68% success rate, not 78% as stated in the paper), and the authors expected a success rate from nasal CPAP of 100% which was unrealistically high. A trial of 60 infants has only 20% power to detect as significant at the 5% level a halving in the rate of failure of extubation of 32% in one group compared with 16% in the other. A trial of 250 infants would be required to have 80% power to detect this same difference.

The conclusions from Chan and Greenough's paper should be that there is a suggestion that nasal CPAP may be superior to headbox oxygen after extubation for babies recovering from acute respiratory distress, and that a multicentre trial of at least 250 babies would be needed to resolve this issue. The reported paper should be considered as a pilot trial to be used as a basis for designing a large multicentre study.

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Drs Chan and Greenough comment:

We agree that only large trial sizes will detect small differences between groups, but such differences may not be clinically relevant. In addition, there are very few treatments that have no associated side effects and large trials are likely to expose a greater number of infants to such problems. In our study use of nasal CPAP resulted in agitation of seven infants with acute respiratory distress and two with chronic respiratory distress and hyperoxia in a further two infants. Our trial thus, importantly, highlighted that nasal CPAP is not appropriate for 'all-comers'. Before embarking on another randomised trial it is therefore important to clearly identify a group of infants who would have minimal side effects from this method of respiratory support. Thus our recommendation is appropriate in the light of present knowledge, that is to individualise the decision to give nasal CPAP after extubation.

Varicella zoster virus infection in pregnancy

EDITOR,—I would like to correct some inaccuracies in the recent annotation by McIntosh and Isaacs on the subject of varicella zoster virus infection in pregnancy.¹ In their table 2, the authors presented data on the proportion of neonates with detectable varicella zoster antibody at birth in relation to the timing of the mother's chickenpox rash before delivery. The source of the data is attributed to a *Lancet* publication by myself and colleagues from the Manchester Public Health Laboratory.² Their table showed that 18/18 infants whose mothers had chickenpox six or more days before delivery had antibody at birth (although the sign \leq was erroneously used to signify 'more than or equal to'). These figures are incorrect, as are the rest of the entries in their table. The actual data from our study are shown in the accompanying table.

The misrepresentation of our results has potentially important implications for the management of perinatal exposure to chickenpox. Based on our study, the Department of Health Joint Committee on Vaccination and Immunisation (JCVI) has recommended that antivaricella zoster immunoglobulin (VZIG) should be given to all infants whose mothers develop a chickenpox rash up to and including seven days before delivery,³ not the five day period recommended by McIntosh and Isaacs. The JCVI also recommends VZIG prophylaxis for infants who are varicella zoster antibody negative who have a close contact with chickenpox during the neonatal period, not just those whose mothers develop a rash up to two days after delivery as recommended by McIntosh and Isaacs. The JCVI recommendation is based on evidence that severe varicella can arise from postnatal infection during the first few weeks of life⁵ and that the presence of passively acquired