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Liverpool and South Sefton health districts was 0.33/1000 live births (that is 16 out of 48 369 deliveries; HM Thomas, unpublished data).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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- 1 Hristeva L, Booy R, Bowler I, Wilkinson AR. Prospective surveillance of neonatal meningitis. *Arch Dis Child* 1993; **69**: 14-8.
- 2 de Louvois J, Harvey D. Infantile meningitis in England and Wales - a two year study. *Arch Dis Child* 1991; **66**: 603-7.
- 3 Shattuck KE, Chonmaitree T. The changing spectrum of neonatal meningitis over a fifteen year period. *Clin Pediatr (Phila)* 1992; **31**: 130-6.
- 4 Franco SM, Cornelius VE, Andrews BF. Should we perform lumbar punctures on the first day of life? *Am J Dis Child* 1993; **147**: 133.

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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- 1 Chan V, Greenough A. Randomised trial of methods of extubation in acute and chronic respiratory distress. *Arch Dis Child* 1993; **68**: 570-2.
- 2 Gardner MJ, Altman DG. *Statistics with confidence*. London: BMA, 1989.

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

antibody is associated with a favourable outcome.⁶

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- McIntosh D, Isaacs D. Varicella zoster virus infection in pregnancy. *Arch Dis Child* 1993; **68**: 1-2.
- Miller E, Cradock-Watson JE, Ridehalgh KS. Outcome in newborn babies given anti-varicella-zoster immunoglobulin after perinatal maternal infection with varicella-zoster virus. *Lancet* 1989; **ii**: 371-3.
- Department of Health. *Immunisation against infectious disease*. London: HMSO, 1992.
- Brunnell PA. Varicella in pregnancy, the fetus, and the newborn: problems in management. *J Infect Dis* 1992; **166** (suppl 1): S42-7.
- Rubin L, Leggadro R, Elie MT, Lipsitz P. Disseminated varicella in a neonate: implications for immunoprophylaxis of neonates postnatally exposed to varicella. *Pediatr Infect Dis J* 1986; **5**: 100-2.
- Baba K, Yabuuchi H, Takahashi M, Ogra PL. Immunologic and epidemiologic aspects of varicella infection acquired during infancy and early childhood. *J Pediatr* 1982; **100**: 881-5.

Dr McIntosh and Professor Isaacs comment:

Our table 2 was in fact obtained from an earlier article published by the same authors in the Communicable Disease Report 4th April 1986 (CDR 86/14), which cannot be used as a reference. We had overlooked the increased numbers of children studied in Dr Miller's 1989 *Lancet* article,¹ and regret this. We do not necessarily agree, however, with her subsequent conclusions.

The severity of neonatal chickenpox depends on the dose of virus as well as the presence or absence of maternal antibody. Epidemiologically most of the severe and fatal cases have been babies whose mother developed chickenpox five or fewer days before delivery. In the paper of Miller *et al* 16 of 19 'severe' neonatal chickenpox cases were babies whose mother's rash was 4 days before to 2 days after delivery.¹ The 1991 Red Book has continued to recommend VZIG for maternal chickenpox at -5 to +2 days,² even though the JCVI has been persuaded to change to -7 days on theoretical grounds.

There have been anecdotal reports of fatal postnatally acquired chickenpox, but there are also fatal cases in apparently immune competent children and adults. It is not known whether the incidence of fatal disease is higher in postnatally infected neonates than later in life, and the Red Book does not recommend VZIG for these babies.

- Miller E, Cradock-Watson JE, Ridehalgh KS. Outcome in newborn babies given anti-varicella-zoster immunoglobulin after perinatal maternal infection with varicella-zoster virus. *Lancet* 1989; **ii**: 371-3.
- American Academy of Pediatrics. *Varicella-zoster infections. Report of the Committee on Infectious Diseases*. 22nd Ed. Illinois: AAP, 1991: 517-24.

Proportion of neonates with antibodies to varicella zoster at birth according to onset of maternal rash²

Onset of maternal rash before delivery (days)	Proportion of babies with detectable antibody*
≤2	0/60
3-5	31/56
6	4/9
7	5/6
8-14	38/38

* >1 arbitrary unit detected by enzyme linked immunosorbent assay.

Echocardiographic assessment of cardiac function in shocked very low birthweight infants

EDITOR,—In their excellent article Gill and Weindling state that neonatal serum electrolyte values are not routinely measured immediately after birth because they, 'invariably reflect maternal levels'.¹ While this statement may be true, and is a frequent excuse for not determining newborn serum electrolyte concentrations early on, obstetricians rarely provide appropriate maternal results. Neonatologists suffer from this lack of information and are frequently surprised at serum electrolyte values eight or 12 hours after birth.

Electrolyte concentrations hold considerable interest for caretakers of sick newborns. Either the obstetricians must regularly provide maternal values at parturition or the neonatologist should measure the baby's concentration shortly after birth. To wait eight or 12 hours because early values reflect maternal levels, yet not to know maternal or newborn levels, is a cop out.

For Gill and Weindling not to have presented such information slightly tarnishes an otherwise excellent, informative report.

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- Gill AB, Weindling AM. Echocardiographic assessment of cardiac function in shocked very low birth weight infants. *Arch Dis Child* 1993; **68**: 17-21.

Drs Gill and Weindling comment:

Unfortunately Dr Scanlon has failed to quote exactly as written in the paper regarding serum electrolyte levels in the first few hours after birth. In our discussion we stated 'Serum calcium and potassium concentrations were not routinely measured in the first few hours after birth as they invariably reflect maternal levels. Subsequent measurements of calcium and potassium after 12 hours of age did not show any difference between the groups.' As the infants did not receive additional calcium and potassium during the first 24 hours we cannot accept that the serum electrolytes were likely to be abnormal at the time of the echocardiogram. To our knowledge, we have not seen any research evidence to suggest that electrolytes should be measured routinely in the first few hours after birth in all preterm infants.

Changes in cerebral artery blood flow velocity after intermittent cerebrospinal fluid drainage

EDITOR,—We agree with the findings of Kempley and Gamsu¹ but dispute their suggestion that these may be used to time cerebrospinal fluid (CSF) drainage in posthaemorrhagic hydrocephalus (PHH).

In a similar study of PHH and ventricular dilatation, we found the same reduction in pulsatility index and increase in mean flow velocity after CSF taps, but because of the very wide range of normal values, were not able to construct an 'action line' to indicate the need for intervention.² In addition, a number of factors unrelated to intracerebral haemodynamics (such as hypercapnia or the presence of a patent ductus arteriosus) may influence the pulsatility index and cerebral blood flow velocity in the ill newborn with

PHH. This is not the case in older children with hydrocephalus in which a clear clinical role for Doppler ultrasound exists.³

We believe that the changes observed by Kempley and Gamsu are acute changes and are of interest in so far as they may reflect the process of autoregulation but that they are unlikely to guide the timing of intervention. Furthermore, it is possible, in the absence of accurate measurements of the angle of insonation, that the flow velocity changes merely reflect a change in vessel distortion with CSF taps rather than a true change in flow velocity.

Intervention should continue to be guided by the rate of head growth and symptoms of raised intracranial pressure⁴ rather than changes in Doppler parameters.

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- Kempley ST, Gamsu HR. Changes in cerebral artery blood flow velocity after intermittent cerebrospinal fluid drainage. *Arch Dis Child* 1993; **69**: 74-6.
- Quinn MW, Ando Y, Levene MI. Cerebral arterial and venous flow velocity measurements in post-haemorrhagic ventricular dilatation and hydrocephalus. *Dev Med Child Neurol* 1992; **34**: 863-9.
- Quinn MW, Pople I. Middle cerebral artery pulsatility with blocked cerebrospinal fluid shunts. *J Neurol Neurosurg Psychiatry* 1991; **55**: 325-7.
- Ventriculomegaly Trial Group. Randomised trial of early tapping in neonatal posthaemorrhagic ventricular dilatation. *Arch Dis Child* 1990; **65**: 3-10.

Dr Kempley and Dr Gamsu comment:

Dr Quinn and Professor Levene suggest that the changes in blood flow velocity (BFV) we observed after intermittent CSF drainage may be due to alterations in the angle of insonation from changes in vessel distortion. This is not the case, as in all measurements we visualised the artery and corrected for the angle of insonation.

We agree that at present, intervention in posthaemorrhagic hydrocephalus should be guided by the rate of head growth and by symptoms and signs of raised intracranial pressure. However, both of our studies demonstrated considerable variations in cerebral artery BFV with this form of management.^{1 2} Compromise of the cerebral circulation by raised intracranial pressure, in combination with other circulatory factors, could cause further cerebral damage in some infants.

The lack of a consistent reduction in cerebral artery BFV in their study² after the onset of ventricular dilatation (ventricular index >2 SD from the mean) may have been because intracranial pressure was not increased at this early stage of ventricular dilatation.

Neither study found a significant correlation between CSF pressure and BFV, perhaps because an infant's ability to maintain cerebral blood flow in the face of raised intracranial pressure depends on a number of factors, such as arterial blood pressure or the presence of a patent ductus arteriosus.

Before dismissing Doppler ultrasound as a tool which could aid decision making in