Low soluble FcRIII receptor demonstrates reduced neutrophil reserves in preterm neonates

Editor,—Studies of human neonate granulopoiesis have been hampered by the lack of a marker of overall neutrophil cell mass. Assumptions about neonate granulopoiesis have therefore largely been extrapolated from rat data. Direct measurement of total neutrophil cell mass (in terms of neutrophils per g body weight) in newborn rats has shown that they have about one quarter the neutrophil mass of adult animals and that their neutrophil mass increases, in response to irritants, by the time they are 4 weeks old.1 In addition, newborn rodents do not have the reserve pool of quiescent granulocytic progenitors, as found in adults, to recruit into production during sepsis. Circumstantial evidence for a similar immaturity of neutrophil production in human neonates comes from the low proportion of quiescent progenitors in cord blood and the frequent occurrence of postnatal neutropenia in preterm infants.2 Some additional insights come from a study of mid-trimester abortuses,3 which showed minimal numbers of neutrophils in haemopoietic tissue before 24 weeks gestation. Until now, direct quantification of total body neutrophil mass in human neonates between 24 weeks and term has remained elusive.

In 1992 we reported4 that preterm neonates born before 32 weeks gestation have very low plasma concentrations of the soluble FcRIII receptor (sFcRIII). sFcRIII is the plasma form of the neutrophil membrane receptor FcγRIII which, together with other membrane receptors, is responsible for binding opsonised partici-

TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>Day no</th>
<th>Total fluids (ml/kg)</th>
<th>Urinary output (ml/kg)</th>
<th>Sodium input (mmol/day)</th>
<th>Sodium output (mmol/day)</th>
<th>Serum sodium (mmol/l)</th>
<th>Weight (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>217</td>
<td>7</td>
<td>3</td>
<td>124</td>
<td>860</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>248</td>
<td>7</td>
<td>3</td>
<td>120</td>
<td>860</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>213</td>
<td>7</td>
<td>10</td>
<td>128</td>
<td>870</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>248</td>
<td>9</td>
<td>14</td>
<td>134</td>
<td>900</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>203</td>
<td>5</td>
<td>15</td>
<td>131</td>
<td>900</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>206</td>
<td>6</td>
<td>15</td>
<td>136</td>
<td>940</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>

PDA, patent ductus arteriosus.
We agree that a randomised trial needs to be undertaken to prove that premedication has the desirable end point of reducing neonatal morbidity, particularly intraventricular haemorrhage.

ASRAR RASHID
Specialist Paediatric Registrar
Neonatal Unit
Birmingham Heartlands Hospital
Bordesley Green, Birmingham B9 5SS
Email: Draraj@limeone.net

MICHAEL WATKINSON
Consultant Neonatologist
Neonatal Unit
Birmingham Heartlands Hospital


Premedication for intubation in neonates

EDITOR,—We were very interested in the recent papers by Blutatua et al1 and Whyte et al2 on the use of premedication for sedative intubation in neonates. It is now well accepted that term and preterm neonates tolerate awake intubation poorly, often exhibiting hypoxia, bradycardia, and systemic and intracranial hypertension during nasotracheal or orotracheal intubation.1 3 Analgesia and sedation are still used infrequently in nurseries for intubation and other “routine”, but invasive, therapeutic or diagnostic procedures.

We recently performed a randomised, double blind, placebo controlled trial to assess whether sedation with midazolam in premature infants would improve physiological stability and the success rate of endotracheal intubation. Eight premature infants underwent 16 intubation procedures after being randomly assigned to one of three groups: I (n = 3), the control group, received placebo only; II (n = 6) received atropine and placebo; and III (n = 7) received atropine and midazolam. Infants could be randomised again to a different group after completion of each intubation procedure. Heart rate, blood pressure, and oxyhaemoglobin saturation were recorded at 10 minute intervals for each infant. The study was terminated when the midazolam data were reviewed early because of concerns over adverse events. The number of episodes of oxyhaemoglobin desaturation around the time of intubation was significantly greater in group III (86%) than in group I (0%; p = 0.01). Cardiopulmonary resuscitation was required in 29% of group III compared with 0% of group II (p = 0.16).

In our trial, premature infants who received midazolam were at increased risk of oxyhaemoglobin desaturation during tracheal intubation. There was also a trend toward an increased need for cardiopulmonary resuscitation in these infants. Although regrettably underpowered because of early termination, our study indicates caution in the use of midazolam as routine premedication for tracheal intubation in premature infants. Further investigation with a larger number of infants is needed to clarify its safety and efficacy profile.

Although we agree that an important goal in neonatal medicine is to minimise pain and stress, more information is needed on the effects of intravenous anaesthetic agents, such as thiopental and methohexitol, in both stable and unstable preterm neonates before these medications can be recommended for routine use. Further randomised controlled trials are needed to help formulate specific premedication guidelines for the variety of noxious procedures that infants undergo in neonatal intensive care units.

DIANE M ATTARDI
Division of Neonatology
Children's Medical Center
Long Branch, NJ 07740, USA
Email: MV14DFT@SOL.COM

DAVID A PAUL
DEBORAH J TUTTLE
Division of Neonatology
Christiania Care Health Services
Newark, DE 19718, USA

JAY S GREENSPAN
Division of Neonatology
Thomas Jefferson University
Philadelphia, PA 19107, USA

Incidence of severe retinopathy of prematurity

EDITOR,—We were interested to read the article of Vyas et al1 on the incidence of severe retinopathy of prematurity (ROP) in 11 neonatal units in five cities in England in 1994. We have published similar data from eight neonatal units in our study (two have been excluded from this analysis as they are neonatal intensive care units). The inclusion of a relatively large number (n = 28) of extremely low birthweight infants is another strength of this study.

Unlike Vyas et al1, we could not find an association between improved survival and the severity of severe ROP. In six of the neonatal units in our study (two have been excluded from this analysis as they are children’s hospitals and have very few small premature infants), survival in infants of < 27 weeks gestation ranged from 51.3% to 68.8%. The percentage with severe ROP for the two units with the lowest and highest survival was 15 (3/20) and 24 (5/21) respectively, while the range of severe ROP in the six neonatal units was 15% (3/20) to 36% (9/25).

In infants of 27–28 weeks gestation, the percentage with severe ROP for the two units with the lowest and highest survival was 7 (4/56) and 3 (2/58) respectively, while the range of severe ROP in this group of infants was 2% (1/50) to 7% (4/56). We therefore agree with Vyas et al1 that there should be no reduction in the upper limit of gestation or birth weight for screening for ROP.

DAVID A TODD
Neonatal Unit
The Prince Anne Hospital
Coxford Road, Southampton
Hants, SO16 6YD,

JOHN KENNEDY
Department of Ophthalmology
Wellmead Hospital
Sydney, NSW, Australia

... (continued from page F161)


Blood pressure standards for very low birthweight infants

EDITOR,—Based on careful invasive blood pressure measurements in a cohort of 61 very low birthweight (VLBW) infants from four tertiary hospitals during the first few hours of life, Lee et al report on blood pressure standards in this population. The quality of the blood pressure readings was assessed using continuous video recordings during the first few hours. The inclusion of a relatively large number (n = 28) of extremely low birthweight infants is another strength of this study.

In an attempt to define normal blood pressure values in a population that by definition is not “normal”, the authors have excluded very ill infants and infants requiring inotropic support. They have also excluded infants who developed intraventricular haemorrhage (IVH) grades III and IV during the first few hours of life. They suggest that the lower limits of mean arterial blood pressure (MAP) for infants between 26 and 32 weeks of gestation are numerically similar to the gestational ages. With the exclusion of infants who developed severe IVH, it became impossible to detect any association between blood pressure and IVH. Decreases in cerebral blood flow may play an important role in the pathogenesis of IVH, and, although MAP is not a reliable parameter to assess cerebral blood flow,3 at least two previously published studies4 5 have shown that the incidence of IVH was higher in infants with lower MAP. Perhaps the authors could indicate how many infants...
with IVH grades III and IV were excluded and what blood pressures were recorded in these infants. For similar reasons, it remains uncertain whether the proposed blood pressure standards are applicable to very ill infants or infants who require inotropic support. It is conceivable that cerebral vascular resistance in sick preterm infants differs from that in the study patients, and consequently the application of the suggested blood pressure standards to sick preterm infants would result in different—and possibly inadequate—cerebral blood flows.

The data presented add to our knowledge on blood pressure in VLBW infants, but do not allow the conclusion that the suggested blood pressure standards are safe for all VLBW infants.

THOMAS M BERGER
Neonatal and Pediatric Intensive Care Unit
Kinderspital Luzern, CH-6000 Luzern 16
Switzerland


Patient triggered ventilation in neonatal respiratory distress syndrome

EDITOR.—Baumer reports the results of a large multicentre study comparing the effects of patient triggered ventilation (PTV) with conventional ventilation (IMV). There appears to be no benefit from PTV compared with IMV in death rate, development of chronic lung disease, pneumothorax rates, and cerebral ultrasound abnormality. In addition, because of an increased trend toward a higher pneumothorax rate, Baumer concludes that, at present, PTV delivered with either the SLE 2000 or the Dräger babylóg 8000 should not be recommended for infants of less than 28 weeks gestation with respiratory distress syndrome (RDS).

However, we are concerned that this may be a premature conclusion given the significant difference in PTV delivery by the two main ventilators and the potential heterogeneity of clinical practice within the different centres involved, despite agreed ventilation protocols. Dimitriou et al showed that neonates and infants trigger a significantly lower proportion of breaths using the SLE 2000, an airway pressure triggered ventilator that provides synchronised intermittent positive pressure ventilation (SIPPV). Attempts to optimise the trigger rate of the SLE 2000 ventilator by increasing pressure sensitivity often results in a high trigger rate as discussed by Baumer. Therefore the PTV modes of the two ventilators are substantially different. This prompts us to ask whether the findings of this multicentre study are only applicable to PTV provided by the SLE 2000? Would there have been a different outcome if all the triggered babies had received SIPPV?

It is not known how many of the 40/213 babies of less than 28 weeks gestation who had pneumothorax were receiving SIPPV. As only 11% (52/465) of all triggered babies ever received SIPPV, we surmise that very few of the 40 were ventilated in this way. Is it fair to conclude that the Dräger babylóg 8000 has a trend to pneumothorax on SIPPV?

In a separate smaller study, Baumer also reports 120 patients in three centres randomly assigned to either the Dräger babylóg 8000 or the SLE 2000 ventilator, and found a non-significant trend towards higher pneumothorax rate, chronic lung disease, and death for the former group. But we are not told how many of the babies were actually on trigger mode (PTV or SIPPV). There would all have been receiving IMV on Dräger babylóg 8000. Therefore is it possible that SIPPV is not being tested?

A further finding was a significantly higher (124/463) of triggered babies that departed from their assigned mode of ventilation, 45 of these failed to trigger their ventilator. Were they all on the SLE 2000 ventilator, as Dimitriou et al would predict?

Finally, we note that 10 of the 22 neonatal units each recruited less than 20 patients over the four year period, one contributing only one patient. Could the technique of PTV ventilation in units contributing so few be different from those enrolling 60–136 patients over the same period, despite prior visits from the trial coordinator? Would a logistic regression for morbidity against number of patients contributed from each unit show that the observed morbidity occurred in units that contributed fewer patients, rather than those using PTV or SIPPV modes?

Given the heterogeneity of the units involved and the significant difference in ventilators used, we think that it is premature to dismiss SIPPV on the Dräger babylóg 8000 in neonates less than 28 weeks gestation with RDS. We agree with Baumer that further studies are required, and extend his conclusion by saying that PTV with the SLE 2000 (n = 411) rather than SIPPV from the Dräger babylóg 8000 ventilator (n = 52) cannot be recommended in this group.

MARGARITA BURMESTER
ANDY PETROS
Intensive Care Unit
Great Ormond Street Hospital
London WC1N 3JH, UK

Dr Baumer responds on behalf of the trial collaborators:

The interest displayed in the trigger ventilation trial by Burmester and Petros is welcome. Their letter raises some important, but not necessarily inappropriately stated, questions that are relevant to the interpretation of the performance of the Dräger babylóg 8000 and the SLE 2000 ventilators.

We did not compare infants with and without IVH but our intention was to define the normal range of blood pressures for very ill infants and those on inotropes, both small infants and this would logically exclude those with IVH and those on inotropes, both small infants and this would logically exclude those with IVH and those on inotropes, both inadequate—cerebral blood flows.

We think that choosing mean arterial pressure of 30 mm Hg as the cut reference in PTV delivered by the two ventilators was not appropriate—cerebral blood flows are heterogeneous in preterm infants or infants who require inotropic support and what blood pressures were recorded in different centres involved, despite agreed ventilation protocols. Dimitriou et al showed that neonates and infants trigger a significantly lower proportion of breaths using the SLE 2000, an airway pressure triggered ventilator that provides synchronised intermittent positive pressure ventilation (SIPPV). Attempts to optimise the trigger rate of the SLE 2000 ventilator by increasing pressure sensitivity often results in a high trigger rate as discussed by Baumer. Therefore the PTV modes of the two ventilators are substantially different. This prompts us to ask whether the findings of this multicentre study are only applicable to PTV provided by the SLE 2000? Would there have been a different outcome if all the triggered babies had received SIPPV?

It is not known how many of the 40/213 babies of less than 28 weeks gestation who had pneumothorax were receiving SIPPV. As only 11% (52/465) of all triggered babies ever received SIPPV, we surmise that very few of the 40 were ventilated in this way. Is it fair to conclude that the Dräger babylóg 8000 has a trend to pneumothorax on SIPPV?

In a separate smaller study, Baumer also reports 120 patients in three centres randomly assigned to either the Dräger babylóg 8000 or the SLE 2000 ventilator, and found a non-significant trend towards higher pneumothorax rate, chronic lung disease, and death for the former group. But we are not told how many of the babies were actually on trigger mode (PTV or SIPPV). There would all have been receiving IMV on Dräger babylóg 8000. Therefore is it possible that SIPPV is not being tested?

A further finding was a significantly higher (124/463) of triggered babies that departed from their assigned mode of ventilation, 45 of these failed to trigger their ventilator. Were they all on the SLE 2000 ventilator, as Dimitriou et al would predict?

Finally, we note that 10 of the 22 neonatal units each recruited less than 20 patients over the four year period, one contributing only one patient. Could the technique of PTV ventilation in units contributing so few be different from those enrolling 60–136 patients over the same period, despite prior visits from the trial coordinator? Would a logistic regression for morbidity against number of patients contributed from each unit show that the observed morbidity occurred in units that contributed fewer patients, rather than those using PTV or SIPPV modes?

Given the heterogeneity of the units involved and the significant difference in ventilators used, we think that it is premature to dismiss SIPPV on the Dräger babylóg 8000 in neonates less than 28 weeks gestation with RDS. We agree with Baumer that further studies are required, and extend his conclusion by saying that PTV with the SLE 2000 (n = 411) rather than SIPPV from the Dräger babylóg 8000 ventilator (n = 52) cannot be recommended in this group.


The contemporary study design allowed a four way randomisation between the two makes of ventilator and the two methods of ventilation. Therefore the possibility of confounding by differences in practice between centres needed to be excluded. If the centres using the SLE as well as the Dräger ventilators were randomised and compared, different outcomes from those using only one make of ventilator, this may have led to inappropriate conclusions being drawn if all infants being ventilated with one ventilator were simply compared with those being ventilated with another. A logistic regression model was therefore used to allow for possible centre effects (as well as other significant factors such as gestation).

With that caveat, I have calculated the numbers from the database giving details of the crude observed rates of pneumothorax in the infants of less than 28 weeks gestation, separately reported for the two makes of ventilator (table 1).

The observed rate of pneumothorax was substantially (but not significantly, χ² 2.8, p > 0.05 < 0.1) higher in the infants ventilated in PTV mode than in IMV mode using the SLE 2000. Although the numbers are small, the observed pneumothorax rate was higher in infants ventilated with the Dräger babylóg 8000 than in those ventilated with the SLE ventilator. If therefore seems somewhat illogical to recommend caution in using
PTV, patient triggered ventilation; IMV, intermittent mandatory ventilation.

Table 1 Numbers of infants of all gestations

<table>
<thead>
<tr>
<th>Mode of ventilation</th>
<th>PTV</th>
<th>IMV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dräger without pneumothorax</td>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>SLE without pneumothorax</td>
<td>154</td>
<td>114</td>
</tr>
<tr>
<td>SLE with pneumothorax</td>
<td>35</td>
<td>14</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mode of ventilation</th>
<th>PTV</th>
<th>IMV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dräger not departing</td>
<td>35</td>
<td>40</td>
</tr>
<tr>
<td>Dräger departing</td>
<td>16</td>
<td>26</td>
</tr>
<tr>
<td>SLE not departing</td>
<td>303</td>
<td>274</td>
</tr>
<tr>
<td>SLE departing</td>
<td>107</td>
<td>14</td>
</tr>
</tbody>
</table>

PTV, patient triggered ventilation; IMV, intermittent mandatory ventilation.

the SLE 2000 in PTV mode in infants less than 28 weeks gestation, but not extend this caution to ventilating infants with the Dräger babyl og 8000.

Given that none of these differences were statistically significant, no clear recommendation can be given. This is why the wording used in the publication was “it might be prudent to avoid…”.

As regards the number of infants departing from their assigned mode of ventilation, several points should be emphasised. The study protocol permitted changing the mode of ventilation at the discretion of the attending clinicians. This was inevitably interpreted differently by each clinical team. Departure from the assigned mode of ventilation was not an intended outcome, and it is evident that this occurred more commonly in the more immature infants and those that subsequently died. High rates of departure from the assigned mode cannot therefore readily be interpreted as evidence of failure of the assigned mode. Table 2 shows the numbers of infants of all gestations departing from the assigned mode of ventilation.

There was therefore a higher crude rate of departure from the assigned mode of ventilation in infants ventilated with the Dräger babyl og 8000, with a similar proportion departing with the Dräger with pneumothorax.

In conclusion, there was no convincing evidence of a beneficial effect of a policy of using PTV in preterm infants with RDS with the ventilators used. Regular attention to staff education on ventilator techniques is recommended.

I would like to use this opportunity to pay tribute to the two trial coordinators (Sue Ellis and Tom Mill), to the trial statistician (David Wright), and to the data monitoring committee (David Field and Diana Elbourne), whose details were inadvertently omitted from the final paper and without whom, together with the trial collaborators, the study would not have been possible.

**Pyridoxine-dependent epilepsy: a suggestive electroclinical pattern**

**Editor,**—There are several problems with describing the electroclinical pattern in pyridoxine-dependent seizures. 1. One is defining the electroclinical features. Until now all published reports (including four of the five cases of Nabbout and colleagues) have described the electroencephalogram (EEG) in neonates who have received other anticonvulsants beforehand. It seems possible that anticonvulsants could affect the EEG, as suggested by the infant with the most pronounced burst suppression pattern in the paper of Nabbout and colleagues. The only other method of assessing the electroclinical pattern is on withdrawal, when we, like others, found that a continuous or intermittent high volt slow wave pattern with or without spikes was typical. 2. It would be very useful to know the EEG features of the patient who did not receive any other drugs before pyridoxine, as this would be the first description of the true electro clinical pattern in pyridoxine-dependent seizures.

This study has shown the use of EEGs in neonatal units. Very few of the neonates reported in the literature or in the UK study had EEGs before receiving pyridoxine. Presumably this reflects difficulties in obtaining EEGs out of hours or the idea is no facility attached to the neonatal unit, as well as the desire to treat without delay. As a result, for some neonatal units it may be difficult to detect a specific electroclinical pattern. A second difficulty is that the clinical features are not very specific. The neonatal presentation can be: as an acute encephalopa thy, followed by later seizures; as seizures accompanied by encephalopathy (both of which introduce a wide differential diagno sis); as seizures alone; or, more unusually, as apparent acute abdominal obstruction or respiratory distress, usually accompanied by irritable behaviour, again followed by seizures. In some reports, seizures have been precipitated by sudden sounds or movements, although some of these could be an exaggerated startle response. Although we too found that a variety of seizures, especially generalised tonic and generalised clonic, occurred in most of our cases, some only had one or two seizure types. In the UK study, five of the 20 definite and probable cases with an early onset were reported to have a single seizure type (unpublished data).

The third concern is that Nabbout and colleagues did not include later presenting cases (older than 28 days) in their report. These also appear to be pyridoxine-dependent as judged by trials of withdrawal and occurrence in siblings. They accounted for three of the 23 definite and probable cases in the UK population study, although a further five had early seizures that responded to routine anticonvulsants and then remained seizure free for several weeks or months. In these, both the clinical and electrical features can differ from neonates. For example, the inter-ictal EEG can be normal, or show focal or generalised spikes or sharp waves with or without high voltage slow waves. The clinical features include recurrent episodes of status and less varied seizure types. Concentrating on a possible neonatal pattern risks overlooking such cases.

As Nabbout and colleagues emphasise, there needs to be a high index of suspicion. Clinically it is important that pyridoxine dependency should be considered in all early childhood seizures, because (a) the baby may be misleading and (b) early treatment does appear to be beneficial.

**Peter Baxter**

Sheffield Childrens Hospital

Western Bank

Sheffield S10 2TH, UK


Parental visiting in neonatal units

**Editor,**—We read with interest the paper by Cuttini et al. 1 Although policy on parental visiting is an easier issue to evaluate, parental participation in decision making, particularly in decisions with strong ethical overtones, is much more complex. It is difficult to evaluate with accuracy, and by its nature is much more controversial. The paper does not stress that data collected from each participating unit, through a structured questionnaire completed by the unit coordinator, represent policies—that is, the intention and stance of each unit towards the particular issue for evaluation. Data collected through questionnaires and interviews involving both unit staff and parents would have provided a better understanding of the actual practice of each participating unit.

No unit from Greece took part in the study by Cuttini et al., but Greece is briefly mentioned in the Discussion, using results from a previous study in which, in a sample
of 38 units from 11 European countries, it was shown that the nine units that imposed visiting restrictions were in France, Greece, Italy, and Portugal.

We would like to provide further information on visiting policy in Greek neonatal intensive care units (NICUs). There are 15, two of which are private; 12 are attached to maternity hospitals and the remaining three are in children’s hospitals and accept direct referrals. Out of one (Agia Kyriakou Children’s Hospital), visiting restrictions are imposed. These allow parents only, and the usual practice is 30 minutes to one hour visiting time in the morning and afternoon (except for mothers). The most common reasons given for imposing restrictions are increased danger of infection and a disruptive effect on the unit.

We conducted a survey, through questionnaire and interview, of parents with a baby who had been cared for in another NICU that imposed visiting restrictions before it was transferred to our NICU and/or parents who had had a previous baby in another NICU that imposed restrictions. The overwhelming majority (98.6%) said that they preferred our liberal policy on visiting. One mother of a preterm baby with bronchopulmonary dysplasia said that “if I had delivered at term I would be with my baby; if I had not delivered prematurely I would also be with my baby (in my womb); now that I have delivered prematurely why can’t I be with my baby?”

We conclude that in Greece there is a demand for unrestricted parental visiting, but most Greek NICUs do not meet this demand for reasons not based on medical or sociological evidence.

It is worth noting that, in Greece, infants beyond the neonatal period have been admitted to children’s wards with their mothers for many years.

H D DELLAGRAMMATICAS NICOLETTA IACOVIDO
NICU, 2nd Department of Paediatrics, University of Athens, Agia Kyriakou Children’s Hospital, 115 27 Athens, Greece


Ureaplasma colonisation and chronic lung disease in neonates

EDITOR.—We read the article by Hannaford et al with interest. We would like to point out that in our recent retrospective analysis, our findings of the colonisation rate of genital mycoplasmas (Ureaplasma urealyticum and Mycoplasma hominis) in the respiratory tract of premature infants of 27% were similar to their study. We also found a higher incidence of chronic lung disease (CLD) in our cohort colonised with genital mycoplasmas.

We are, however, intrigued by the implication of a “protective effect” of Ureaplasma colonisation on respiratory distress syndrome (RDS) in this study. The hypothesis that this may be related to the “stimulatory effect of subacute intrauterine infection on lung maturation.” is interesting but unsubstantiated. Current evidence suggests that the sicker infant with RDS has an increased early inflammatory response and a higher rate of CLD. In the present study, the incidence of RDS in Uu colonised infants was lower—but their incidence of CLD at 36 weeks was higher. Were there other factors—for example, increased incidence of PDA, more IV fluid use, that predisposed these infants to develop CLD? Another issue is that in the multivariate analyses, Uu colonisation was a significant risk factor for CLD only in singleton infants, but the relationship did not hold true when all infants were analysed. Based on these observations, we wonder if the “protective effect” is real or a statistical aberration? More research needs to be done to study this “protective effect” of Uu colonisation on RDS before any conclusions can be drawn.

The treatment of Uu colonisation was not discussed in this paper. In our experience, erythromycin alone was not effective in clearing the organism from the respiratory tract. We found a short course of postnatal steroids alone or in combination with erythromycin more effective. 1 We wonder if infants receiving postnatal steroids were confounders in the discrepancy between the incidence of RDS and CLD.

VINEET BHANDARI
Department of Paediatrics, Albert Einstein Medical Center, Philadelphia, PA 19141, USA
NAVEED HUSSAIN
Department of Paediatrics, University of Connecticut Health Center, Mailcode 2203, Farmington, CT 06030–2203, USA


Dr Gilbert et al respond:

EDITOR.—We thank Drs Bhandari and Hussain for their interest in our paper. We too were intrigued by the apparently contradictory effects of ureaplasma colonisation on the lungs of affected infants and acknowledge that our hypothesis is unsubstantiated. The possibility that a subacute intrauterine infection could stimulate endogenous surfactant production is a plausible explanation for the significantly lower incidence of respiratory distress syndrome (RDS) in these infants. The fact that intrauterine infection is low grade, may also mean that delivery is delayed for long enough for exogenous steroids to take effect.

The development of chronic lung disease (CLD) is dependent on many factors, and, in our study, it correlated less closely with ureaplasma infection than did RDS. We assumed that other effects of multiple gestation outweighed those of ureaplasma infection on the development of CLD in twins. Presumably, the lower rate of RDS in ureaplasma-infected singleton infants reduced their risk of CLD, directly or indirectly. If so, there must be other respiratory insults severe enough to offset this effect. We were unable to identify factors associated with CLD from RDS and ureaplasma infection. In particular, the incidence of PDA did not differ between infants with and without CLD.

We postulate that the low grade inflammatory effect of intrauterine ureaplasma infection could cause significant irreversible lung damage and predispose to CLD, as well as stimulating the production of surfactant. The outcome is unlikely to be affected by erythromycin therapy after birth, except in the minority of infants in whom there is frank pneumonitis, with progression after birth.

We have not studied the effects of postnatal steroids, but this is unlikely to be a significant confounding factor, since in our study the time the study was done, steroid therapy was not given until about four weeks of age, when CLD was already established.

Although we agree that further research is needed to confirm our findings, we believe that the inverse relationship between ureaplasma colonisation and RDS was too strong to be dismissed as a statistical aberration.

GILBERT
Centre for Infectious Diseases and Microbiology, Institute of Clinical Pathology and Medical Research, Westmead Hospital, Westmead NSW Australia 2145

Editor’s note

References 22–30 of the paper by Hannaford et al were incorrect, and each correlate with the number below in the text. Thus reference 22 in the reference list corresponds with reference 21 in the text, and so on. This correction appears online [dcm.bmjournals.com/cgi/content/full/fetalneonatal/81/F3/162/DC1].

The journal would like to apologise for this error.

CORRECTION

The authors of the paper “Risk adjusted and population based studies of the outcome for high risk infants in Scotland and Australia” Arch Dis Child Fetal Neonatal Ed 2000;82:118–123 have asked us to publish the following corrected version of table 6. The authors apologise for the error.

<table>
<thead>
<tr>
<th>Relative risk of neonatal death</th>
<th>500–999 g</th>
<th>1000–1499 g</th>
<th>500–1499 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative risk of neonatal death</td>
<td>5% confidence interval</td>
<td>5% confidence interval</td>
<td>5% confidence interval</td>
</tr>
<tr>
<td>Scotland vs Australia 1993–94</td>
<td>1.24</td>
<td>1.09–1.42</td>
<td>1.20</td>
</tr>
<tr>
<td>Scotland vs Australia 1993–96</td>
<td>1.48</td>
<td>1.35–1.63</td>
<td>1.34</td>
</tr>
<tr>
<td>England and Wales vs Scotland 1994</td>
<td>1.15</td>
<td>1.07–1.24</td>
<td>1.18</td>
</tr>
<tr>
<td>England and Wales vs Australia 1993–96</td>
<td>1.25</td>
<td>1.19–1.32</td>
<td>1.23</td>
</tr>
</tbody>
</table>