LETTERS TO THE EDITOR

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The editors will decide, as before, whether to also publish it in a future paper issue.

A national review of neonatal resuscitation programmes for midwives

EDITOR,—A considerable number of babies (67%) have no standards of achievement set for resuscitation training. Standards were characterised by proficiency in basic life support, clinical scenarios, and theoretical knowledge of neonatal resuscitation. Resuscitation training was compulsory for midwives in 132 (72%) units. Most (88%) of the 196 maternity units that responded have some form of resuscitation programme available for midwives. However, the programme in 42% of these units does not directly follow the Neonatal Life Support Course, recommended by the UK Resuscitation Council. Moreover, 67% of programmes have no established standards. The average period of reassessment in these units is nine months. This interval may be too long because skill retention has been shown to be lost within six months of a neonatal resuscitation programme.

The specific needs of UK midwives to provide basic neonatal life support have not been objectively evaluated, in contrast with the United States and Canada.1 There are no directives from governing bodies for midwives to attend mandatory neonatal life support updates. Moreover, the national availability of specific neonatal resuscitation programmes for midwives is not known.

A standardised written and telephone questionnaire survey of all national maternity units (n = 245) was undertaken. The questionnaire primarily examined duration, structure, and assessment strategies of the resuscitation programmes for midwives.

All 245 maternity units were surveyed by written and telephone questionnaires; 196 responded (80%). Of these, 172 (88%) have some form of resuscitation programme available for midwives. The resuscitation programmes have been in existence for a mean (SD) of 3.7 (2.6) years (range 0.5–20). The programmes involve on average 1.9 main trainers (range 1–5), including senior midwives, paediatricians, and resuscitation training officers. There are pronounced structural differences between the available resuscitation programmes. Those in 100 (58%) units closely follow the Neonatal Life Support course guidelines (UK Resuscitation Council). The programmes in the remaining 72 (42%) units are variably incomplete in their evaluation of neonatal basic life support. Of the units currently not following standard guidelines, 61 (94%) expressed a desire to change. Of the units with resuscitation programmes, 116

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Placement of neonatal central venous catheter tips in the right atrium: a practice to be avoided?

EDITOR—Following the recent media interest in pericardial tamponade complicating the use of percutaneous central venous catheters in neonatal patients, we wish to alert readers to our experience. Our previous policy was to accept right atrial placement of percutaneous central venous catheter tips. This was in line with published recommendations and is still considered acceptable practice in some units in the United Kingdom, in contrast with practice in the United States. Between 1996 and 1997, we had five cases of neonatal pericardial tamponade, three of which resulted in death. All were associated with right atrial tip position, confirmed by angiography, echocardiography, or chest X-ray. We have now changed our unit policy to avoid placement of catheter tips in the right atrium, and instead place them in the superior or inferior vena cava. In addition, to allow for the possibility of catheter migration, we recommend that catheter tips should lie at least 0.5 cm outside the cardiac outline on chest radiograph in small infants, or 1.0 cm outside in larger infants. Although this position carries a small risk of thrombosis or hydrothorax, these complications are more benign than pericardial tamponade, which has a mortality of 65%. We recommend that placement of a percutaneous central venous catheter tip in the right atrium should no longer be accepted. In addition, we suggest that catheters that display angulation, curvature, or looping within the right atrium carry a particularly high risk of pericardial tamponade and demand urgent action. Although this issue has been the subject of correspondence in the RCPCH email discussion list, where the consensus was to avoid right atrial tip position, we believe there is a current need for a wider debate about current practice in the United Kingdom.

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Newborns have unique confounding factors regarding the TIR-F ratio

EDITOR—Sweet et al investigated the transferrin receptor (STIR) and, for the first time in neonates, transferrin receptor-log ferritin (TIR-F) ratio in a prospective series of cord blood taken from term infants and their mothers. They are to be congratulated on completing another piece of the complex jigsaw that is fetal and neonatal iron metabolism. STIR and TIR-F were increased in iron deficient mothers, but not in their infants. The authors discuss some length the translational (not transcriptional as stated in the discussion) control of intracellular ferritin synthesis. They measured serum ferritin, which is a glycosylated form of L-ferritin, and has been shown to correlate with intracellular iron in the absence of confounding factors. However, serum ferritin is secreted in response to a wide variety of stimuli, including, for example, inflammation and shows gender differences in newborns. Of these differences, serum ferritin may not accurately represent tissue iron stores. It has already been reported that STIR does not correlate with other measures of iron metabolism in the newborn. Moreover, because it is highly expressed by reticuloocytes and other immature erythroid cells, with or without iron deficiency. The high sensitivity and specificity of the TIR-F ratio in adults is based upon their relationship in iron deficiency in the absence of factors that might otherwise elevate STIR levels. With both variables subject to these confounding factors in the neonate, I do not agree with the author’s assertion that the TIR-F index “gives a measure of iron requirements in relation to iron availability” in this unique population.

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Changes in plasma creatinine in first 72 hours of life

EDITOR—Recently, Miall et al have reported a rapid rise in serum creatinine in the first 48 hours of life in neonates. But have we noticed in our clinical day to day practice that this rise is transient and may not be clinically significant. To confirm this, we looked at the initial serum creatinine levels on a stable group of term neonates admitted to the neonatal intensive care of King Fahd Hospital of the University, Al-Khobar, Saudi Arabia.

Neonates with congenital anomalies, perinatal asphyxia, and those requiring ventilatory support were excluded. The serum creatinine levels were measured together with electrolytes by using an automatic analyser (Dimension, Delaware, USA), which were then recorded and analysed using the Statistical Package for the Social Sciences (SPSS) at peak level. The mean, standard deviation and statistical significance.

Out of thirteen neonates, seven (53.8%) had an increase in their plasma creatinine on the second day while four (30.7%) had a
The drop to 0.44, as compared with day 1, does not necessarily indicate renal failure or kidney impairment. In our preliminary results, we noted that the rise in creatinine in the first 48 hours was transient and by the third day, the mean serum creatinine had returned to the preterm infant range. However, a significant variation in the results was observed. Most of the creatinine levels (92%) had returned to levels below 0.44 mg/dl by the third day, the mean serum creatinine of the 13 cases was 0.44 mg/dl, compared with preterm infants.

Between the ages of 13 and 92%, the mean age was 0.68 mg/dl, with a range of 0.44–1.2 mg/dl. Of 13 cases (92%), there was a significant variation in the results. However, a significant variation in the results was observed. Most of the creatinine levels (92%) had returned to levels below 0.44 mg/dl by the third day, the mean serum creatinine of the 13 cases was 0.44 mg/dl, compared with preterm infants.

Haemoglobinopathy as a cause of nucleated red cells in the fetus and neonate

**EDITOR,—We are interested in the article by Hermansen on the causes of peripheral nucleated red cells in newborn children and would add another differential diagnosis to this finding.**

In the last decade, we have discovered two families affected by haemoglobin disorders where the diagnosis was suspected by the presence of high numbers of nucleated red cells in neonatal and cord blood tests. In neither family was there a known history of haemoglobin disorders. The families were referred to the Indian neonatal and childhood health services, and a newborn with nucleated red cells was found to have haemoglobin H disease. The child now presents with thalassaemia intermedia, but because of the difficulty in predicting the clinical course of these disorders, it is not yet clear whether they will become transfusion dependent. Although this is highly likely for two individuals, one in each family.

The first recognised child in Family 1 was born in 1991. A blood test performed because of jaundice on the third day of life showed Hb 160g/l. Other causes of erythroblastosis were excluded. Haemoglobin analyses on the parents showed that the mother was heterozygous for Indian version/ deletion b-thalassaemia, while the father was a compound heterozygote for db-thalassaemia and Haemoglobin Headington.3 This child and two other children are homozygous for db-thalassaemia. The eldest child seems more severely affected and has been transfused twice, following infections.

The second family presented in 1996 when their first son was found at birth to have 2000NRBC/100 WBC. Other causes having been excluded, haemoglobin studies revealed only the existence of b-thalassaemia trait (codon 16bO) in the father. The boy is now anaemic, has thalassaemic binoxygosis of the skull and spleenomegaly, and looks as if he will need a transfusion programme. A brother, born in 1999, had 983NRBC/100 WBC in his initial blood test, and has also inherited his father’s haemoglobin pattern. It is likely that this family is showing dominant b-thalassaemia, although recent studies suggest there may be a co-inherited aldolase deficiency, akin to aldolase, from the mother (J Porter, personal communication).

We hope this report may help in the investigation of other families.

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Neonatal paroxetine withdrawal syndrome or actually serotonin syndrome?

**EDITOR,—We would like to comment on the article “Neonatal paroxetine withdrawal syndrome” in the March 2001 issue of the journal.**

The authors describe what they have called “neonatal paroxetine withdrawal syndrome”. However, the syndrome reported in the 4 neonates appears to be more consistent with serotonin toxicity, rather than withdrawal of paroxetine.

The literature to date contains one large series, two similar case reports with fluoxetine4 and two case reports with paroxetine.5 In the fluoxetine cases, the syndrome was not described as a withdrawal phenomenon. In the first, a neonate born to a mother on fluoxetine had jitteriness, irritability, tachypnoea, temperature instability, tremors, increased muscle tone, and a hyperactive Moro reflex. All except the last of these are clinical features seen in serotonin toxicity in adults using selective serotonin uptake inhibitors (SSRIs) therapeutically or in overdose.1 The neonate in this case had fluoxetine levels that were measurable initially and which fell as symptoms resolved.

In the two cases with paroxetine, the syndrome is referred to as a withdrawal phenomenon. However, the time course and symptoms were similar to those of serotonin excess.

In the case reported by Stiskal et al7 the neonates developed the features soon after birth and they resolved over a period of days. In case 2 an increased serum paroxetine level was reported in the infant. The level was too low to detect by day 15, supporting a toxicity syndrome, rather than a withdrawal phenomenon. Similarly, in case 4 there was a raised serum paroxetine level at the time of the adverse effects. Serum paroxetine levels have been positively related to serotonin toxicity in adults.

The features of case 4 may also have been exacerbated by the use of opiates in the delivery room. Pethidine is a well recognised cause of serotonin toxicity in conjunction with a serotoninergic agent.8

By March 2001, there were 13 reports to the Australian Drug Reaction Advisory Committee classified as “withdrawal syndrome

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Table 1

<table>
<thead>
<tr>
<th>Child</th>
<th>Date of birth</th>
<th>Age (days)</th>
<th>Hb (g/dl)</th>
<th>WBC (corrected)</th>
<th>NRBC/100WBC</th>
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<tr>
<td>ZR (male)</td>
<td>20/07/90</td>
<td>3</td>
<td>11.1</td>
<td>13.0</td>
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<td>MR (female)</td>
<td>16/08/91</td>
<td>5</td>
<td>12.7</td>
<td>24.0</td>
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<tr>
<td>ZR (female)</td>
<td>09/11/96</td>
<td>9</td>
<td>13.3</td>
<td>9.0</td>
<td>100</td>
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<tr>
<td>HA (male)</td>
<td>16/07/96</td>
<td>1</td>
<td>13.7</td>
<td>11.7</td>
<td>2000</td>
</tr>
<tr>
<td>AA (male)</td>
<td>02/07/99</td>
<td>3</td>
<td>14.2</td>
<td>13.9</td>
<td>983</td>
</tr>
</tbody>
</table>

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Table Differences in the mean creatinine in first 72 hours

<table>
<thead>
<tr>
<th>Number of samples</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>Time (SD)</td>
<td>Range</td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
<td>-------</td>
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</tr>
<tr>
<td>13</td>
<td>0.64 (0.18)</td>
<td>(0.3–0.8)</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>0.68 (0.20)</td>
<td>(0.3–1.0)</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>0.44 (0.13)</td>
<td>(0.3–0.7)</td>
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</tr>
</tbody>
</table>
neonatal” in conjunction with maternal use of an SSRI. On perusal, many appear to describe serotonin toxicity. We have also been involved with the management of a neonate, born to a mother following a sertraline overdose, who exhibited features of serotonin toxicity. In this case there was a single maternal ingestion 1 hour before delivery and therefore no earlier foetal exposure to cause withdrawal.

We are concerned about the increasing use of the term “neonatal withdrawal syndrome” in symptomatic neonates being born to mothers on SSRIs. This may prompt the use of SSRIs themselves to treat the condition with the potential to increase toxicity. The condition should be correctly referred to as “neonatal serotonin toxicity” or, less specifically, poor neonatal adaptation secondary to serotonergic agents.

Authors’ response

EDITOR,—Isbister and colleagues point out that the described syndrome is due to a hyper serotonergic state, rather than a lack of serotonergic effect, as the term “withdrawal” suggests. We agree that this issue must be clearly solved because of the significant implications in the clinical management of some of the patients, especially concerning the role of continued breast feeding. At the same time, we are unsure whether we have sufficient data to declare that this is a hyper serotonergic condition. When we started summarising our experience as a report, we debated what terminology should be used to describe our patients. The term “SSRI discontinuation syndrome” was considered as it simply describes the temporal relationship between the dose and the syndrome. However, we opted for “withdrawal” because of its common use in similar cases in the literature. For example, a report by Kent and Laidlaw describes a full term healthy boy born to a mother on sertraline who was breast fed for three days. A day after weaning he developed agitation, poor feeding, constant crying, insomnia, and an enhanced startle reaction.

These effects intensified over 48 hours then subsided. The time course in this case strongly suggests a withdrawal reaction. Our 2 patients had therapeutic serum concentrations of the drug. However, we do not know the concentrations prior to the presentation, hence the interpretation of the data is not as simple as Isbister and the colleagues indicate.

We think that the conditions we described resulted from a hypo-serotonergic state due to withdrawal. However, the possibility of functional excess of serotonin cannot be ruled out from the clinical assessment alone as there is considerable overlap between the two entities. The cause of the discontinuation syndrome in adults also remains incompletely understood.

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2. Kent LSW, Laidlaw JDD. Suspected congenital serotonin syndrome in adults also remains incompletely understood.

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