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A national review of neonatal resuscitation programmes for midwives

**Editor,—**A considerable number of babies with no obstetric or neonatal at risk factors require help in establishing respiration at birth. This may range from tactile stimulation to bag and mask ventilation to endotracheal intubation.

Midwives in the United Kingdom are primarily involved in the initial resuscitation of newborn babies in delivery units and at home. There is a national lack of neonatal resuscitation training in the United Kingdom, with inadequate provision of neonatal life support skills remaining an acknowledged contributory factor to perinatal death.1,2 There are no directives from governing bodies for midwives to attend mandatory neonatal life support training sessions. Encouragingly, 84% of units currently not following the UK Resuscitation Council guidelines expressed a desire to change accordingly.

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**Hypernatraemia: why bother weighing breast fed babies?**

**Editor,—**Hypernatraemic dehydration is associated with cerebral oedema, intracranial haemorrhage, hydrocephalus, gangrene, and death,3 but is notoriously difficult to detect clinically. It is accepted in paediatric practice that weighing is an essential part of the assessment of an infant’s hydration.

In Bristol, one neonate a month is admitted with hypernatraemic dehydration secondary to delayed recognition of inadequate lactation. We believe that this is a result of the reluctance of midwives to weigh breast fed infants.

Five neonates admitted after they became unwell from dehydration secondary to lactation failure are described (table 1). Assessment of lactation and hydration had raised no concern. Four of five of these mothers were primigravidas and four of five gave up breast feeding despite encouragement to continue.

The weighing practices of midwifery teams and the opinion of neonatologists throughout the South West Region were compared by telephone survey. Four of 13 community midwifery units always or often weighed babies on day 3, 4, or 5, and the other nine routinely weighed for the first time since birth on day 7 or 10. Twelve of 14 consultant neonatologists thought that adequate inpatient care would be provided by routinely weighing on day 3, 4, or 5 after birth (midwifery practice v consultant opinion, p = 0.006; χ² test).

Hypernatraemic dehydration as the result of failure to establish lactation is well described, although not recently in this country. Associated factors include first time motherhood, poor support of lactation, and failure to monitor excessive weight loss.2,4 Identification of excessive weight loss can swiftly identify breast feeding problems, enabling appropriate lactation support to be given and prevention of hospital admission.

In common with the Oregon Academy of Pediatrics and others, we recommend that breast fed infants should be weighed between 72 and 96 hours after birth when normal weight loss is at its maximum.

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Table 1 Clinical details of five neonates presenting with hypernatraemic dehydration

<table>
<thead>
<tr>
<th>Infant</th>
<th>Maternal parity</th>
<th>Birth weight (kg)</th>
<th>Day 3 maternal weight (kg)</th>
<th>Weight loss (%)</th>
<th>Plasma sodium (mEq/l)</th>
<th>Plasma area (cm)</th>
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<tr>
<td>1</td>
<td>0</td>
<td>3.430</td>
<td>8</td>
<td>25</td>
<td>168</td>
<td>25</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
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<td>7</td>
<td>24</td>
<td>172</td>
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<tr>
<td>3</td>
<td>0</td>
<td>3.500</td>
<td>19</td>
<td>138</td>
<td>158</td>
<td>46.3</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>3.630</td>
<td>20</td>
<td>150</td>
<td>150</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>2.420</td>
<td>13</td>
<td>157</td>
<td>157</td>
<td>6.1</td>
</tr>
</tbody>
</table>
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 one complication associated with this practice in the United Kingdom, in contrast with practice in the United States. Between 1993 and 1997, we had five cases of neonatal pericardial tamponade, three of which resulted in death. All were associated with right atrial tip positioning. We believe that angulation, curvature, or looping of the line is the cause of this complication. 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,1 these complications are more benign than pericardial tamponade, which has a mortality of 65%.2,3 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 positioning, we believe there is a pressing 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 discussed 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.1 However, serum ferritin is secreted in response to a wide variety of stimuli, including, for example, inflammation and shows gender differences in newborns.2-4 In the circumstances, 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, and primarily 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.5 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, Miail et al1 have reported a rapid rise in serum creatinine in the first 48 hours of life in neonates. But we have noticed in our clinical day to day practice that this rise is transient and may not be clinically significant. To confirm this, we studied a limited number of neonates born at term and in our previous study of preterm infants we found no gender differences in contrast to the results published by Tamura et al.2 Our figure for cord ferritin levels at term (listed first as mean + SD) in ferritin infants is almost identical to Tamura et al (164 + 106 µg/l v 166 + 110 µg/l), but our value for male infants is higher (160 + 97 µg/l v 123 + 71 µg/l). We doubt if there are real gender differences in fetal ferritin levels. Therefore, we are still of the opinion that TIR-F index is a measure of iron requirements in relation to iron availability in the fetus and newborn as in adults and children.

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Reply

Editor,—We thank Peter Reynolds, but feel that our use of the term post-transcriptional is quite adequate to describe the regulation of intracellular iron metabolism was correct. Iron regulatory elements (IREs) are stem cell loop structures of several key messenger RNA (mRNA) encoding proteins of iron metabolism. IREs can be located in the 5′ region—for example, ferritin, or 3′ region—for example, transferrin receptor, of the untranslated region of the mRNA. In relative iron deficiency, through interaction of the IREs with iron responsive proteins, transferrin uptake increases because the transferrin receptor mRNA is stabilised, whereas ferritin storage of iron decreases because translation of ferritin mRNA is blocked. These are clearly post-transcriptional, not post-translational events. The reciprocal regulation of the transferrin receptor and ferritin have recently been expertly reviewed by Hentze and Kuhn.3

We agree that serum ferritin is increased in response to inflammation but the infants that we studied were born at term following normal pregnancies. All the babies were healthy and did not require neonatal care. We think that it is unlikely that inflammation or other stimuli affected our serum ferritin values. Furthermore, in this study and in our previous study of preterm infants we found no gender differences in contrast to the results published by Tamura et al.2 Our figure for cord ferritin levels at term (listed first as mean + SD) in ferritin infants is almost identical to Tamura et al (164 + 106 µg/l v 166 + 110 µg/l), but our value for male infants is higher (160 + 97 µg/l v 123 + 71 µg/l). We doubt if there are real gender differences in fetal ferritin levels. Therefore, we are still of the opinion that TIR-F index is a measure of iron requirements in relation to iron availability in the fetus and newborn as in adults and children.

The drop to 0.44, as compared with day 1 of validity to our preliminary results. However, a range for plasma creatinine during the first month of life. Arch Dis Child 1983;58:212-15. The study demonstrated a trend of fall in the first 72 hours. This reflected the improvement in the renal function and GFR. The improvement in the GFR has shown to be a function of postconceptional age, reflected by lower creatinine levels in term and near term infants as compared with preterm infants. We noted that the rise in creatinine in the first 72 hours was transient and by the third day; the mean serum creatinine of the cohort had dropped to a significant level, 0.64 mg/dl to 0.44 mg/dl, p = 0.04 (table 1). 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 160NRBC/100WBC. Other causes of erythroblastosis were excluded. Haemoglobin analyses on the parents showed that the father was a compound heterozygote for db-thalassaemia and Haemoglobin Headington. 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 166B) in the father. The boy is now anaemic, has thalassaemic bissociation of the skull and sphenomegaly, and looks as if he will need a transfusion programme. A brother, born in 1999, had 983NRBC/100WBC 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).

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

Editor,—We are interested in the article by Hermans’ on the causes of peripheral nucleated red blood 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 blood tests. In neither family was the potential for significant haemoglobin disorders suspected. The families concerned were Indian Asian in origin and the marriages were consanguineous. The children now present 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 dependant, 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 160NRBC/100WBC. Other causes of erythroblastosis were excluded. Haemoglobin analyses on the parents showed that the father was a compound heterozygote for db-thalassaemia and Haemoglobin Headington. 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.

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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 fluoxetine and two case reports with paroxetine. 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. The neonate in this case had fluoxetine levels that were measurable initially and which fell as symptoms resolved.

In the two case reports with paroxetine, the syndrome is referred to as a withdrawal syndrome rather than a withdrawal phenomenon. However the time course and symptoms were similar to typical of serotonin excess.

In the case reported by Stisal et al the neonates developed the features of serotonin syndrome 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 serotonin 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 serotonergic agent.

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

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>
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</table>
neonatal" in conjunction with maternal use of an SSRI. However, 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

EDITORS,—Isbister and colleagues point out important issues in defining the syndrome we and others described. Their argument is that the described syndrome is due to a hyper serotoninergic state, rather than a lack of serotonin 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 serotoninergic 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 weaned 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 hyp-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.1

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References


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