LETTERS TO THE EDITOR

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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 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 (84%) expressed a desire to change. Of the units with resuscitation programmes, 116 (67%) have no standards of achievement set for resuscitation training. Standards were characterised by competence in basic life support, clinical scenarios, and theoretical knowledge of neonatal resuscitation. Resuscitation training was compulsory for midwives in 132 (72%) units. Midwives are reassessed on average every 9.2 (5.8) months (range 6–24), with 148 (86%) units holding a logbook of attendance. There are regional differences in the availability of resuscitation programmes (range 77–100%), existence of standards of achievement (range 1–50%), and existence of compulsory resuscitation programmes (range 50–92%). Overall, North West hospitals have high scores in the above three categories stated. Currently, no individual region has the highest scores for all the categories stated.

This is the first national survey examining neonatal resuscitation programmes for midwives. 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 guidelines 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.[3]

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.[4] In addition, there is a collective call for consistent skills attainment, nationally and internationally.[5] The availability of resources and personnel may contribute to regional differences in resuscitation programmes. Continued structural differences in neonatal resuscitation programmes will further exaggerate differences in local and national practices. Hence, the need to establish uniform standards in neonatal resuscitation and for mandatory hospital trust support not only in organising suitable resuscitation programmes, but also in ensuring compulsory attendance by midwives at these essential 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,[1] 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 the optimum care would be provided by routinely weighing on day 3, 4, or 5 after birth (midwifery practice *v* consultant opinion, $p = 0.006$; χ^2 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 early weight loss.[2] 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 American 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.[3]

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Table 1 Clinical details of five neonates presenting with hypernatraemic dehydration

Infant	*Maternal parity*	*Birth weight (kg)*	*Day next weighed*	*Weight loss (%)*	*Plasma sodium*	*Plasma urea*
1	0	3.430	8	25	168	25
2	0	2.120	7	24	172	34.8
3	0	3.799	6	19	158	46.3
4	0	3.630	6	20	150	10
5	3	2.420	4	13	157	6.1

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[1–3] and is still considered acceptable practice in some units in the United Kingdom, in contrast with practice in the United States.[4] 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 position, accompanied by angulation, curvature, or looping of the line.[5] 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,[6] 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 the caval position carries a small risk of thrombosis or hydrothorax,[2 7] these complications are more benign than pericardial tamponade, which has a mortality of 65%.[8 9] 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 pressing need for a wider debate about current practice in the United Kingdom.

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Newborns have unique confounding factors regarding the TfR-F ratio

EDITOR,—Sweet *et al* investigated the serum transferrin receptor (STfR) and, for the first time in neonates, transferrin receptor-log ferritin (TfR-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.

STfR and TfR-F were increased in iron deficient mothers, but not in their infants. The authors discussed at some length the translational (not transcriptional as stated in the discussion) control of intracellular ferritin synthesis.[1] 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.[2] However, serum ferritin is secreted in response to a wide variety of other stimuli, including, for example, inflammation and shows gender differences in newborns.[3] Under these circumstances, serum ferritin may not accurately represent tissue iron stores.

It has already been reported that STfR does not correlate with other measures of iron metabolism in the newborn,[4] mainly because it is highly expressed by reticulocytes and other immature erythroid cells, with or without iron deficiency.

The high sensitivity and specificity of the TfR-F ratio in adults is based upon their relationship in iron deficiency in the absence of factors that might otherwise elevate STfR levels.[5] With both variables subject to these confounding factors in the neonate, I do not agree with the author's assertion that the TfR-F index "gives a measure of iron requirements in relation to iron availability" in this unique population.

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Reply

EDITOR,—We thank Peter Reynolds, but feel that our use of the term post-transcriptional 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.[1]

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 well at birth 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[2] and in our previous study of preterm infants[3] we found no gender differences in contrast to the results published by Tamura *et al*.[4] Our figure for cord ferritin levels at term (listed first as mean + SD) in female infants is almost identical to that of 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 TfR-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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Changes in plasma creatinine in first 72 hours of life

EDITOR,—Recently, Miall *et al*[1] 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 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 relayed by the reporting computer system (Ulti-view, Los Angeles, USA). Serum creatinine was available for the first 72 hours on a limited number of neonates, as most of the selected babies were stable within the first 48 hours of life and there was no need for extra serum electrolyte and creatinine measurements. Out of all the newborns admitted during the three month study period who fulfilled the inclusion criteria, 13 neonates had serum creatinine measurements available for the first 72 hours. These readings werenoted down and were analysed using the SPSS statistical package to calculate the mean, standard deviation and statistical significance.[2]

Out of thirteen neonates, seven (53.8%) had an increase in their plasma creatinine on the second day while four (30.7 %) had a

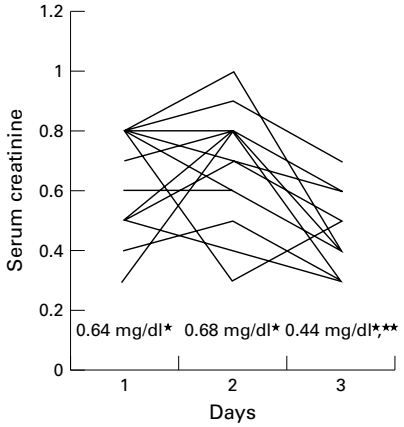

*Figure 1 Graphic representation of changes in creatinine in first 72 hours of life. *mean creatinine values; **p = 0.04, compared with day 1. To convert to µmol/l multiply by 88.4.*

Table 1 Differences in the mean creatinine in first 72 hours

Number of samples	Time	Serum creatinine (mg/dl)	
		Mean (SD)	Range
13	Day 1	0.64 (0.18)	(0.3–0.8)
13	Day 2	0.68 (0.20)	(0.3–1.0)
13	Day 3	0.44*(0.13)	(0.3–0.7)

*The drop to 0.44, as compared with day 1 of 0.68, was statistically significant, p = 0.04.

reduction. The remaining two (15.3%) had no change in their creatinine. After 72 hours of life, 12 out of 13 (92%) of the cases had a reduction in the creatinine (fig 1). 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 study demonstrated a trend of fall in serum creatinine level by 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.[3–5]

We noted that the rise in creatinine in first 48 hours was transient and by the third day most of the creatinine levels (92%) had dropped down. One could argue about the sample size of our study. The sample size was restricted as no extra blood was extracted for the purpose of study. The results with 12 out of 13 cases (92%) suggest that there may not be wide variation in the results. However, a larger study will provide more reliability and validity to our preliminary results.

In conclusion, caution should be exercised in interpretation of serum creatinine levels in the first 72 hours of life. A raised serum creatinine level in early newborn period does not necessarily indicate renal failure or kidney disease.

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

EDITOR,—We are interested in the article by Hermansen[1] 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 mother was heterozygous for Indian inversion/deletion db-thalassaemia, while the father was a compound heterozygote for db-thalassaemia and Haemoglobin Headington.[2] 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 bossing of the skull and splenomegaly, 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,[3] although recent studies suggest there may be a coinherited 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.[1] 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,[2] two similar case reports with fluoxetine[3 4] and two case reports with paroxetine.[5 6]

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.[3] 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.[7 8] 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 phenomenon. However the time course and symptoms were similarly typical of serotonin excess.

In the cases reported by Stiskal *et al*[1] 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.[8]

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.[7]

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

Table 1

Child	Date of birth	Age (days)	Hb (g/dl)	WBC (corrected)	NRBC/ 100WBC
ZR (male)	20/07/90	3	11.1	13.0	22
MR (female)	16/08/91	3	12.7	24.0	160
ZR (female)	09/11/96	1	13.3	9.0	950
HA (male)	16/07/96	1	13.7	11.7	2000
AA (male)	02/07/99	1	14.2	13.9	983

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.

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Authors' response

EDITOR,—Isbister and colleagues point out important issues in defining the syndrome we and others described.[1 2] Their argument is that the described syndrome is due to a hyper serotonergic 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 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[3] describes a full term healthy boy born to a mother on sertraline who was breast fed for three weeks. 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.[4]

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