

## LETTERS TO THE EDITOR

### Oxygen saturation and retinopathy of prematurity

EDITOR,—The observations of Tin *et al*<sup>1</sup> have led them to suggest that babies may have better overall outcomes when unit policies aim at oxygen levels of 70–90%, much lower than current practice in most NICUs. While I would support their call for further well designed research into this question, I have major concerns that this concept of beneficial hypoxia might creep into clinical practice, and even be extended to the older survivors. The authors are clearly aware of the limitations of their study. There are obviously many possible alternative reasons for the differences in outcome between the nurseries; table 2 of the study suggests widely divergent policies on a number of issues apart from oximetry levels. There are no data supplied regarding the actual oximetry levels maintained in the nurseries, which makes conclusions about the safety of a saturation of 70% rather speculative.

My main concern is the potential risk to older babies with chronic lung disease who might once again be subjected to chronic hypoxia. Since the more widespread acceptance that babies with chronic lung disease require similar oxygen levels to their more fortunate brethren we have largely abolished the high first year mortality in these babies, and the pulmonary hypertension which was previously seen. One observational study of differing oximetry levels within a single unit confirmed the high risk of even mild chronic hypoxia in this group of infants,<sup>2</sup> showing a high risk of apparently life threatening events in the hypoxic infants.

While there is continued uncertainty about the optimum oximetry levels in the early life of a preterm baby, there is no justification for maintaining subnormal levels of oxygen in babies beyond 34–36 weeks of age with chronic lung disease, and I trust that this paper will not encourage such practice.

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- 2 Iles R, Edmunds A. Prediction of early outcome in resolving chronic lung disease of prematurity after discharge from hospital. *Arch Dis Child* 1996;74:304–8.

### Oxygen saturation and retinopathy of prematurity—Authors' response

EDITOR,—We are happy to make it clear that we have never suggested that hypoxia is “beneficial” to babies with chronic lung disease. Indeed in describing our own practice we said, quite specifically, that “babies who were at least 8 weeks old (and it should be remembered that all our babies were born more than 12 weeks early), and whose retinal vasculature was mature, received liberal oxygen supplementation.” We would, however, remind Dr Primhak that those babies in the recent STOP-ROP trial who were given

enough supplemental oxygen to maintain a saturation of 96–99% (to see if this reduced the severity of the retinopathy they had already developed) developed significantly more pulmonary problems than those only given enough oxygen to maintain a saturation of 89–94%.<sup>1</sup>

The idea that oxygen is always a “good thing” dies hard. Iles and Edmunds<sup>2</sup> showed that babies with a saturation below 90% in air at discharge were more likely to have a frightening colour change, apnoeic episode and/or sudden change in muscle tone during the subsequent three month study period, but they did not show that that this risk was reduced by giving oxygen. There is equally little objective evidence that offering sustained supplemental oxygen actually does reduce the incidence of troublesome pulmonary hypertension.

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### Two sacred cows of neonatal intensive care

EDITOR,—I read the descriptive study of Tin *et al*<sup>1</sup> with considerable interest. In essence it challenges two sacred cows of neonatal intensive care, whether intra-arterial monitoring is necessary, and what is the appropriate PaO<sub>2</sub> at which to nurse critically ill babies.

#### ARTERIAL MONITORING

They do not give us accurate details of arterial catheter use. There is a hint that they are used for the first few days before resorting to SpO<sub>2</sub> and capillary measurements. Nor do they tell us what analgesia is used for multiple capillary samples.

A fundamental principle of neonatal intensive care is minimal handling, and indwelling arterial catheters allow all samples to be taken with no or minimal disturbance, and if the catheters are umbilical, they can also be used safely for virtually all infusions including TPN. Furthermore, as opposed to oscillometric techniques, they allow accurate blood pressure recordings.

Surprisingly, the literature, and my own clinical experience is that the serious complications of UAC are much more common in term infants, and within 48–72 hours of insertion, so that 28/52 babies leaving UAC in situ for many days is unlikely to have a major impact on the putative complication rate of this procedure that induces anxiety in neonatologists.

Local analgesia for heel pricks is surprisingly ineffective even if applied for (impractically) long periods prior to puncture. If general analgesia with, say, morphine is being used the manipulation involved in capillary sampling is still likely to result in the changes in oxygenation (and thus intracerebral haemodynamics with potentially damaging

sequelae), that were so graphically illustrated in many papers in the 1970s and 1980s when continuous PaO<sub>2</sub> and tcPO<sub>2</sub> monitoring became available.

To inflict frequent painful capillary sampling procedures on an unstable 25/52 800 G neonate in the first week of life where blood gas sampling may be necessary at least 2–3 hourly could at best be described as ill judged, at worst negligent.

#### APPROPRIATE PaO<sub>2</sub>

As they rightly say, running babies at SpO<sub>2</sub> levels of 70–90 (PaO<sub>2</sub> approximately 25–45mmHg, 3.3–6 kPa) is an old idea, and I remember spirited arguments about it with the late great Sir Peter Tizzard during my training in the mid 1960s.

It is interesting, but not new, that if you keep babies cyanosed, ROP is rare. Many anecdotal papers from the late 1950s during the panic over oxygen therapy showed that rigid restriction of oxygen dramatically reduced ROP, but probably increased mortality.<sup>2</sup> Although the validity of papers reporting on an association between oxygen restriction in the late 1950s and 1960s and mortality have been challenged, it remains an anxiety.

It remains in this study with an overall mortality of 52%. We do not know the proportion of babies off 23/24 weeks in the study, but it is likely to be relatively small. Contemporary studies reported by Lorenz from the USA<sup>3</sup> give an overall mortality of 38% in babies of compatible gestation and year of birth, falling to 26% in those of 25, 26, and 27 weeks. The figures for Cambridge were virtually identical. Therefore, unless the Newcastle units are overloaded with 23/24 week babies the overall mortality rate with “physiological” oxygenation (has Blairite spin even penetrated neonatology?) is worryingly high.

Reporting their cerebral palsy rate is irrelevant. Improved neonatal care has in general (depressingly) little effect on cerebral palsy rates; what changes is the number of survivors and the numbers dying.

Importantly, cerebral palsy is only one part of the problem of surviving ELBW. Equally worrying is their under performance at school in childhood and adolescence. In the past, when children with cyanotic congenital heart disease were either inoperable or operated on only in early childhood, prolonged early hypoxaemia of the level used by Tin *et al* was associated with subsequent cognitive defects.<sup>4</sup> The Newcastle group has a distinguished track record of long term follow up studies, and hopefully the babies in this study will be followed until adolescence. However, until such data show that babies kept at 3.3–6.0kPa for days and weeks during a vulnerable period for brain development do as well as those kept adequately oxygenated, I would regard the practice as described by Tin *et al* as of unproven benefit and possibly dangerous.

Finally, the marked restriction of oxygen therapy was, at best, experimental. Was a protocol for this study presented to the local research ethics committee? If not, why not?

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- 1 Tin W, Mulligan DWA, Pennefather P, Hey E. Pulse oximetry, severe retinopathy and outcome at one year of babies of less than 28 weeks gestation. *Arch Dis Child* 2001;84:F106–10.

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### Two sacred cows of neonatal intensive care—Authors' response

EDITOR,—I am glad to have a chance to respond to Dr Robertson's assertion that the care of the babies nursed using oximeter settings of 70-90% was "negligent", since I was responsible for these children, but time and space does not allow a full response. Neither does space allow me to respond to the criticism implicit in your own introductory statement that such care "breaches BAPM guidelines".

Dr Robertson says the cerebral palsy rate is "irrelevant", but parents might not agree. Parents might also be glad that, while 4 children monitored using an oximeter alarm set at 88-98% went blind, no child in the other group went blind. They might also be glad that half were off the ventilator in 7 rather than 22 days, and out of oxygen in 4 rather than 10 weeks. The NHS might be equally grateful for the reduction in cost such an approach delivers. Post delivery growth in the conservatively managed group was only retarded half as much as in the comparator group, even though only a quarter ever received any parenteral nutrition. I am happy to leave parents to be the judge of whether this was "negligent" care.

Babies were not "kept at 3.3-6.0 kPa for days and weeks"; target saturation delivered an arterial partial pressure of 5-11 kPa, but alarm settings were more generous than this to discourage staff from adjusting the ventilator every time saturation transiently fell below 80%. Nor was blood pressure monitored by oscillometry (a technique that is known to be unreliable),<sup>1</sup> as a proper reading of the paper would reveal. Dr Robertson mistakenly calls our survival rate our mortality rate, compares survival for mostly black American with that of our white English children, compares survival to discharge with survival to one year, and says nothing about the reliability with which gestation was documented.<sup>2</sup> The same issue of your journal contains a better review of survival.<sup>3</sup> We have every intention of following these children, but felt it would be wrong to wait ten years before reporting the above findings.

Dr Robertson mentions the outcome of a study of 38 children offered corrective surgery for transposition 6 months to 5 years after birth.<sup>4</sup> Those operated on early had a better cognitive outcome, but Dr Robertson does not mention the fact that these children had a mean saturation of 68% before operation, and that 8 had a history of acquired central nervous system damage.

However, the main thrust of Dr Robertson's letter is that lack of an arterial line subjected these babies to unnecessary pain. This overlooks the fact that morphine was given during early care, while early extubation greatly reduced the total number of blood samples eventually taken (as the differing transfusion needs confirm). Samples were not taken every 2-3 hours initially, but every 6-8 hours. In fact, Dr Robertson and I are at one in agreeing that minimising pain is a very



Figure 1 The modified nasopharyngeal airway in place.

valid reason for inserting an umbilical artery line in babies as immature as this; the limited use of lines was only mentioned because these have been considered necessary in the past to minimise the risk of severe retinopathy—a belief for which there is absolutely no controlled trial evidence.

Finally, Dr Robertson asks if this approach ever had ethics committee approval. It did not, because it was merely a continuation of the non-invasive approach initiated by my predecessor Dr Neligan in the mid 1970s, aided by the arrival of transcutaneous gas monitoring. Neither was the introduction of pancuronium in Dr Robertson's own unit<sup>5</sup> placed before an ethics committee.

I can only conclude that someone ought to cull the two sacred cows Dr Robertson has been worshipping (along with all the other animals recently culled in the UK). In the absence of any other evidence based information, we need a proper controlled trial to address these issues.

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### Using a modified nasopharyngeal airway in Pierre Robin syndrome

EDITOR,—EDITOR,—Masters *et al* describe how a modified endotracheal tube can be used as a nasopharyngeal airway in infants with Pierre Robin syndrome.<sup>1</sup> We describe further modifications made to overcome

some problems which we encountered in using the technique in one of our patients.

In the original description the protruding part of the airway is cut into four strands and the upper one cut off. We found the remaining strands rather thick, so cut them to half the width. We found that leucoplast tape was the only tape that held the strands in place with no additional benefit resulting from the use of Tinc Benz. The strands rubbed badly where they curved over the edge of the nostril. To overcome this a piece of suction catheter (8F) of just sufficient length to extend over the lateral and medial walls of the nostril is tied transversely across the tube with a 3/0 silk tie (fig 1). This lifts the three strands off the edge of the nostril and prevents any rubbing.

In our patient blockage of the airway occurred after formula but not breast milk feeds. It is therefore advisable to suction the airway after each feed. We used a suction catheter with graduation marks enabling insertion no further than the tip of the airway. If inserted further the pharyngeal stimulation usually caused vomiting.

If a nasogastric tube is also required this can be taped to one of the strands rather than the face. The airway was changed every four to six days, immediately before a feed and alternating between nostrils. Using 1% lignocaine drops and smearing the tube with lignocaine jelly reduced crying time after insertion.

Compared to the use of an unmodified tube with a large connector attached to the end, we feel that the technique described by Masters *et al* is far superior as it enables the child to lie prone and is less liable to get knocked or blocked through kinking. We suggest that the modifications we have described will further improve the acceptability of the technique.

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### Staff perception of pain on a neonatal intensive care unit

EDITOR.—It is now widely accepted that even the most preterm babies experience pain. This is difficult to measure and a number of clinical scales have been developed to make this assessment as objective as possible. Without the use of objective scales, the assessment of pain can become very subjective. We have measured staff perceptions of pain experienced by babies in different clinical situations in a neonatal intensive care unit. Clinical scenarios were presented to nursing and medical staff of the Exeter Neonatal Unit, and they were asked to score on a visual analogue scale the severity of pain they felt a baby experienced in these situations. The scale ranged from no pain to extreme pain on a 10 cm line and staff were asked to mark a point on the line that represented their assessment of the likely level of pain, and they were also asked whether they thought analgesia was necessary for the baby. There were six clinical scenarios:

- a Guthrie test on an awake term baby using a spring loaded Autolet device;
- a ventilated baby of 28 weeks gestation in no obvious distress with normal blood gases;
- a 35 week gestation baby of a diabetic mother who had four attempts at intravenous cannula insertion;
- a term baby with respiratory distress syndrome who developed a pneumothorax needing chest drain insertion;
- a 37 week gestation baby who had grazing of the scalp following a failed ventouse and difficult forceps delivery;
- a 27 week gestation baby who needed a lumbar puncture as part of a septic screen.

The response to the questionnaire was anonymised. Sixty six questionnaires were distributed to 21 doctors and 45 nurses. Fifty six (85%) responded, of whom 18 were doctors (eight men, 10 women) and 38 were nurses (three men, 35 women). The doctors comprised senior house officers, specialist registrars, staff grade, consultants, and nursing staff of sisters, senior nurses, staff, and nursery nurses. The overall scenario score (calculated by totalling the score for each scenario) was significantly higher for nurses (mean (SD) = 28.5 (6.8)) than for doctors (mean (SD) = 35.8 (6.8);  $p < 0.01$ ). The scenario score was significantly higher ( $p < 0.01$ ) for nurses in four of the six clinical scenarios. The two scenarios in which the difference was not significant were the 28 week gestation ventilated baby and the baby with a grazed scalp, although in both situations the mean score was higher for nurses than doctors. In all scenarios, more nurses than doctors thought that analgesia was necessary but this was only statistically significant for the baby needing lumbar puncture (97% *v* 77%;  $p = 0.03$ ).

We feel this questionnaire study of our unit highlights important differences in perception of pain between doctors and nurses. Does it reflect a sex difference in the composition of the two groups? Are doctors distancing themselves from the pain that often they inflict when performing practical procedures or are they more aware of potential side effects of the analgesics used? It would be interesting to explore the reasons for these differences.

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### Use of the black area on the tubetip for rapid estimation of insertional depth of endotracheal tubes in neonates: a potential hazard

EDITOR.—I would like to report on a premature neonate who was intubated unilaterally as a result of improper use of the black area at the endotracheal tubetip.

At 29 weeks gestational age, a 1020 g boy was born by emergency caesarean section to a mother who presented with preeclampsia. He was intubated immediately for signs of severe respiratory distress with a 3.0 mm ID tube via the nasotracheal route by the resident on call. The black area of the tube was inserted full length through the vocal cords with the upper rim positioned at the level of the vocal cords. Breath sounds were equally distributed on auscultation. The tube was fixated with adhesive tape at the 10 cm mark at the nose. A thoracic *x* ray revealed that the tubetip was located in the entrance of the right main stem bronchus. The tube was withdrawn 1.5 cm and refixated at 8.5 cm at the nose, after which exogenous surfactant was instilled for treatment of grade 3 idiopathic respiratory distress syndrome. The ensuing clinical course was uneventful and the infant was discharged with signs of mild bronchopulmonary dysplasia several weeks later.

During the evaluation of this incident it was found that the resident who intubated had been taught at another institution that a position of the upper rim of the black area at the level of the vocal cords would ensure a proper insertional depth. However, the tubes at this other institution were produced by a different manufacturer. This prompted us to measure the actual length of the black area on the neonatal size endotracheal tubes of four major manufacturers. As shown in table 1, the length of the black area varies among tubes from different manufacturers. One manufacturer has adjusted the length of the black area to the size of the patients for which a particular tube size is indicated. The others added a black area of a certain length merely to allow for rapid visualisation of the tube in the oropharyngeal space during the intubation procedure. Indeed, the black area of the tubes that are in use at our institution have a fixed length of 30 mm, regardless of tube size and, thus, patient size. The distance from the vocal cords to the carina of a neonate of 1000 g is approximately 30 mm.<sup>1</sup> This explains the endobronchial position after full length insertion of the black area of the endotracheal tube through the vocal cords in our patient. The

Table 1 Length of black area at the tubetip of endotracheal tubes for neonatal use as produced by four major manufacturers

Tube (ID)	2.5	3.0	3.5	4.0
Rüsch	20	20	20	30
Portex	20	24	30	35
Vygon (st)	17	19	—	—
Vygon	25	25	25	25
Mallinkrodt	30	30	30	30

Tube ID and length of black area expressed in mm. st, surfactant tube.

equal distribution of breath sounds that was used in this case to determine the correct tube position has been shown to be an unreliable parameter for this purpose in neonates.<sup>2</sup>

In conclusion, this report illustrates that caution is required in the use of the black area at the tubetip for rapid estimation of insertional depth of endotracheal tubes in neonates.

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### Respiratory distress syndrome and antenatal corticosteroid treatment in premature twins

EDITOR.—Randomised, placebo controlled trials of antenatal corticosteroid administration have not shown a significant reduction in the incidence of respiratory distress syndrome (RDS) in premature twins.<sup>1</sup> Subsequent retrospective studies examining the effect of steroids on twin pregnancies have shown conflicting results.<sup>2,3</sup>

Further to our recent article,<sup>4</sup> we have investigated the relation between respiratory distress and antenatal corticosteroid treatment in premature twins from the same historical cohort selected from the Australia and New Zealand Neonatal Network (ANZNN) 1995 database. To reflect best possible clinical practice, the analysis was restricted to the effects of an optimal steroid course (two doses of corticosteroids given, the first dose of which was received more than 24 hours and less than eight days before the infant's birth) compared with no steroid treatment.

As shown in table 1, treatment with antenatal steroids resulted in a significantly lower incidence of RDS and surfactant use. The reduction from 18% to 11% in the risk of mortality was not significant ( $p = 0.08$ ). Recent advances in obstetrics and neonatology could explain the absence of an antenatal steroid associated reduction in mortality.<sup>5</sup> There was no statistically significant association between optimal steroid use and the outcome measures of days of intermittent positive pressure ventilation, days of oxygen, oxygen at 36 weeks corrected gestational age, severe intraventricular haemorrhage, or the number of proven infection episodes. Gestation, sex, race, and birth order did not modify the association between antenatal steroid treatment and RDS incidence.

The sample examined in this study is over twice the size of the most recent retrospective analysis, which reported no antenatal steroid associated reduction of RDS in twins.<sup>3</sup> However, the reduction in RDS incidence observed in our study is less than that seen in singleton infants (odds ratio 0.35, 95% confidence interval 0.26 to 0.46).<sup>3</sup> Optimal steroid treatment may be less effective in multiple gestation pregnancies because the increased volume of distribution in these mothers may reduce the plasma level of steroids to which the fetuses are exposed.<sup>1</sup>

Table 1 Effect of antenatal steroids on respiratory distress syndrome (RDS) in premature twins

Outcome measure	Optimal antenatal steroids		No antenatal steroids		Odds ratio (95% CI)	p Value
RDS	184/310	59%	79/106	75%	0.49 (0.27 to 0.91)	0.02
Surfactant use	162/333	49%	67/108	62%	0.58 (0.34 to 0.99)	0.05
Mortality	35/334	11%	20/110	18%	0.53 (0.26 to 1.08)	0.08

Results are number of twin infants affected over number of infants at risk, also expressed as a percentage. Odds ratio and p values were produced by logistic regression with standard errors adjusted for within pair correlation.

Data used for this study came from the Australia and New Zealand Neonatal Network.

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## BOOK REVIEW

**The Neurological Assessment of the Preterm and Full-term Newborn Infant.** L Dubowitz. (Pp 167; £35.00.) Cambridge University Press, 2000. ISBN 1898683158.

Progress in the management of disease in the newborn has carried with it a recognition of the substantial risk of injury to the immature nervous system. The aspiration to localise and prognosticate from neurological signs in the early newborn period is easily understood. The problem is that the signs available to be discerned are in themselves usually insufficient to allow precision. In addition, the child grows and develops, the range and complexity of skills are constantly changing, and the manifestations of the lesion(s) alters, or may become silent, often to reappear later as a different but nevertheless highly significant impairment.

The evaluation of the newborn nervous system was originally based upon concepts learnt from adult neurology. The baby was seen as demonstrating little or no cortical or cerebellar activity and the study of primary reflexes predominated. The approach of adult neurology, with emphasis on localisation of the lesion, becomes less applicable in the younger child. In the newborn period, focal insults to the brain will often give rise to generalised disturbances and, contrarily, generalised disturbances may show focal deviations. Recognition of these phenomena has led to a progression from the concept of a localisation based neurology to one which sees the infant displaying a neurological/behavioural repertoire. Over the past several decades Saint Anne Dargassies, Prechtel, Amiel Tison, Brazelton, Dubowitz, and others have, through meticulous study, done much to illuminate this area. Through these studies, awareness of the importance of the behavioural state of the baby, as well as the more detailed neurological items has evolved.

A second problem in this area, particularly in relation to research studies, has been the development of a systematic newborn neurological examination which is reliable and

repeatable. This has been the subject of the two editions of this work. The first, published in 1981, gave a detailed, easily understood and applied system for the neonatal neurological examination. The current edition brings that work up to date. New material is presented, refinement of the scheme has occurred, and the examination is described. Items which were less discriminatory of pathology from the 1981 version have been withdrawn and, following the work of Prechtel, more emphasis is placed on the analysis of general movements. There is a further post neonatal to two year old infant neurological examination proforma presented briefly at the end of the text.

The text is essentially a manual on the application of this neurological examination scheme. It is easy to follow and the segments of the examination are presented clearly with excellent photographs and line drawings of each manoeuvre. There is also a useful addendum ("cautionary tales") to each section of the examination, giving guidance on possible pitfalls and sources of error. There is a lot of very useful information on the variations in findings in term and preterm infants, and particularly the changes in the neurological features of preterm infants as they grow towards term. There follows a section on the development of an optimality score from the observed items of the assessment. This section deals with the results of a survey of 224 normal term infants. In this study each item of the scheme was plotted, and centile values (and thereby optimality scores) were computed. This provides quantification of the assessment, a sense of the range of findings to be expected, and can be useful in correlating lesions observed on neuro imaging with clinical findings. Chapter six deals with the scheme in relation to findings in infants with recognised brain lesions.

The book is not designed to be a text of neonatal neurology and readers looking for discussion of neurological disease states will be disappointed. As a description of a comprehensive and easily applied system of neonatal neurological examination the new edition succeeds admirably.

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## Two sacred cows of neonatal intensive care— Authors' response

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