LETTERS TO THE EDITOR

Individualised pulse oximetry limits in neonatal intensive care

EDITOR,—Gupta et al have successfully demonstrated that they were unable to accurately predict PaO₂ from saturation monitoring even after standardising from a previous measurement. The rest of the conclusions presented in their discussion are however based upon interpretation of other research findings which is not further supported by their own study. They correctly point out that the poor relation between SpO₂ and PaO₂ is related to differing proportions of fetal haemoglobin, PCO₂, and acid–base balance. This begs a question, which their discussion fails to address, on whether the PaO₂ or the SpO₂ is the most useful index of oxygenation. It is certainly the case that normal in utero PO₂ is within a range which they would describe as “hypoxic”. On the other hand, in the presence of 100% fetal haemoglobin, a saturations monitor should, in these circumstances, correctly indicate adequate saturation.

The authors also remark that transcutaneous oxygen monitoring is “a better way of non-invasively assessing PaO₂”. They provide no evidence for this remark. It is certainly a common experience to find a saturation monitor alarming high when a transcutaneous monitor is apparently recording a normal or even low PO₂ because of an undetected poor contact. It is also not the case that transcutaneous oxygen monitoring, particularly on the extremely premature infant, is entirely non-invasive.

In the long run, the purpose of oxygen monitoring is to detect degrees of hypoxia which are likely to cause acidosis or tissue damage and levels of hyperoxia which may risk retinopathy of prematurity. To date there would appear to be no study comparing different measurement methods with respect to these outcomes. However, the authors’ own discussion of the reasons for the poor correlation between SpO₂ and PaO₂ provides an excellent theoretical argument in favour of the former over the latter!

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Dr Yoxall and Dr Shaw respond:

Dr Clifford has raised the important question of whether PaO₂ or SpO₂ is the best index of arterial oxygenation. The answer to this question is, of course, unknown and the aim of our study was not to attempt to provide an answer. Most of the work defining hypoxia and harmful hyperoxia in neonates was performed in the era prior to pulse oximetry and therefore defines these situations in terms of partial pressure rather than oxyhaemoglobin saturation. The guidelines for good practice in the management of neonatal respiratory distress syndrome published by BAPM and RCP state that arterial blood sampling is the “gold standard” for assessing arterial oxygenation. In the absence of evidence to the contrary, we would agree with this.

Pulse oximetry is widely used during neonatal intensive care. Our study has shown that it is not possible to accurately predict PaO₂ from SpO₂ even after standardising from a previous measurement. The information provided by measurements of PaO₂ and SpO₂ is different and should not be interpreted as interchangeable. As SpO₂ monitoring is non-invasive, non-inconvenient, and has a rapid response time, it useful for monitoring trends and particularly in detecting episodes of sudden deoxygenation.

Monitoring of PaO₂ is possible using transcutaneous monitoring and this is a better way of continuously monitoring PaO₂ than trying to extrapolate from the SpO₂ signal. The ease with which pulse oximetry can be applied has led to the virtual abandonment of transcutaneous monitoring by many units. There are technical difficulties with transcutaneous monitoring as pointed out by Dr Clifford, but these can be overcome if the staff caring for the babies are familiar with the technique and use it on a routine basis. The anecdotal experiences of those units that continue to use transcutaneous monitoring as part of their clinical routine is that it remains an extremely useful technique.

The purpose of maintaining adequate arterial oxygenation is to provide oxygen to meet the metabolic demands of the baby, prevent pulmonary hypertension, and avoid oxygen toxicity. We do not have a satisfactory method of defining what constitutes adequate oxygenation during intensive care at present and it is necessary to take into account other variables, such as haemoglobin concentration or tissue perfusion, which also determine oxygen delivery when we assess our patients.

Dr Slack and Dr Schapira respond:

We thank Dr Slack for his comments about our report. He is quite correct that neither we nor any of those authors who have previously described these events have provided any evidence that it is either the pertussis component of the diphtheria/tetanus/whole cell pertussis vaccine or its endotoxin content that is responsible for these reactions. That is why we described it as “the presumed cause”.

It is possible that any of the vaccine components or adjuvants are responsible. It may simply be a response to pain, although this seems unlikely. However, given the evidence of reduced local and systemic reactions with acellular pertussis vaccines in term infants compared with the UK whole cell vaccine, it seems plausible that the pertussis component may be involved.

He is partially correct in stating that the way to answer this would be to conduct a three way randomised trial between placebo, acellular (DTaP), and whole cell pertussis (DTP) vaccines. In fact, it would require multiple randomisations between Hib, DT, DTaP, one, two, three, and five component DTaP vaccines, and placebo. Even if the use of a placebo were ethically acceptable, which we believe would not be the case, the low incidence of these events would make the number of infants required for such a study impossibly large.

We are, however, conducting a multicentre study to determine the incidence of apnoea following immunisation using a three component acellular vaccine. Finally, we do not accept that we have joined the ranks of those who have shaken confidence in the vaccination programme.


The question is not whether preterm infants should be immunised against pertussis but when and with what vaccine.

Dr McClure responds:
We agree, and indeed stated in our own paper1 that cisapride has been shown in children to improve symptoms of gastro-oesophageal reflux disease and to hasten both gastric emptying and gastrointestinal transit time. We believe that it is dangerous to assume that the immature gut of the preterm infant will react in the same manner. We further believe that our study has the strongest methodology. We directly examined the effect of cisapride on gastrointestinal motility in the preterm infant. As stated in our discussion, we did not measure gastric reflux and so cannot comment on the efficacy of cisapride for this condition. However, in view of our findings, until there is published evidence in a peer reviewed journal of cisapride’s efficacy for this condition, we would therefore conclude that it should be contraindicated as recommended by the Medicines Control Agency.

We do not believe that the choice of hydroxypropylmethyl cellulose as a placebo, given at the “same volume” as cisapride; however, the actual quantity administered is not clear. Cellulose derivatives are commonly employed as laxatives, where it is proposed that they act by absorbing water, so softening the faeces and increasing stool volume. This in turn stimulates faecal propulsion. Clearly, depending on the dose of hydroxypropylmethyl cellulose used, the choice of this compound as a placebo is nonsensical as there could be a marked impact on gastrointestinal transit time. From the publication it is also not clear why gastrointestinal motility was measured after three days dosing; it is likely that any cathartic effect from a laxative would be less marked after more prolonged treatment time.

The manufacturer had recommended against the use of cisapride in premature infants because of concern that the metabolic pathway of cisapride may not be fully developed, and so overestimates ductal significance which would question the duct, and so overestimates transcardiac shunting back into the lungs through the ductus arteriosus where LVO becomes the sum of SBF and volume of blood shunting back into the lungs through the duct, and so overestimates SBF. While Zhang et al define ducts in their study babies as insignificant, we would question the validity of the criteria used to make this definition. We have never seen shunting only in diastole, chamber enlargement is an inconsistent sign of ductal shunting which only develops after day one, and shunt velocity has little relation to shunt size during week one. In fact, the left to right velocity often decreases as the duct constricts and the shunt diminishes in size. Bidirectional shunting is also usually predominantly left to right.

There is much in the data presented by Markiewicz and Vandenplas, which give the indications for the use of cisapride in neonates, we published a Medline search using the search terms “cisapride” and “infant,” and found no references. This is discussed only in three randomised controlled trials of cisapride versus placebo in neonates.1 4 One other study compared cisapride with placebo in infants, but only a subgroup of this study population were preterm infants.


1 Markiewicz M, Vandenplas Y. Should cisapride have been “blacklisted”? Arch Dis Child Fetal Neonatal Ed 2000;82:F3–4.


Mechanism of blood pressure increase induced by dopamine in hypotensive preterm neonates

EDITOR,—The paper of Zhang et al on the effects of dopamine relies on the assumption that left ventricular output (LVO) is a measure of systemic blood flow (SBF). This is not true in the presence of any shunt through the ductus arteriosus where LVO becomes the sum of SBF and volume of blood shunting back into the lungs through the duct, and so overestimates SBF. While Zhang et al define ducts in their study babies as insignificant, we would question the validity of the criteria used to make this definition. We have never seen shunting only in diastole, chamber enlargement is an inconsistent sign of ductal shunting which only develops after day one, and shunt velocity has little relation to shunt size during week one. In fact, the left to right velocity often decreases as the duct constricts and the shunt diminishes in size. Bidirectional shunting is also usually predominantly left to right.

There is much in the data presented by Zhang et al to suggest that these ducts were highly significant; firstly, they selected a population at high risk for a significant duct,
and secondly they measured a mean diameter of 2.9 mm. We showed that this measure is the most accurate predictor of early haemodynamic significance and that preterm ducts over 2 mm in diameter, with very few exceptions, have a haemodynamic impact. In this haemodynamic milieu, LVO is actually a measure of pulmonary blood flow, and right ventricular output becomes the better measure of SBF, but even this can be confounded by the common finding of left to right atrial shunting. That this haemodynamic impact is often present from the very early postnatal period is emphasised in fig 1 which is of a 5 hour old infant of 26 weeks gestation, in whom we measured an LVO of 350 ml/min per kg but a right ventricular output (RVO) of 90 ml/min per kg. This baby had an unrestricted duct (2.6 mm) with a low velocity (0.7 m/s) but high volume left to right shunt. In other words LVO was overestimating SBF by a factor of over 300%. This is not an unusual finding.

This means that the changes in LVO in response to dopamine documented by Zhang et al. may have occurred in the systemic circulation but, equally, could have occurred in the pulmonary circulation. The same uncertainty applies to changes in calculated vascular resistance. In other words, LVO may have increased or decreased solely because dopamine has changed the volume of the ductal shunt back into the lungs.

Early preterm ductal shunting should not be assumed to be inconsequential, and interpretation of early postnatal measures of either right or left ventricular output in preterm infants should be approached with caution.

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Figure 1. Doppler measures taken from a 26 week infant at 5 hours of age. (A) High velocity flow (about 1.0 m/s) in the ascending aorta representing a left ventricular output of 350 ml/min per kg. (B) Low velocity flow (about 0.2 m/s) in the pulmonary artery representing a right ventricular output of 90 ml/min per kg. (C) Low velocity (about 0.7 m/s) high volume laminar left to right flow through an unrestricting duct.


Dr Zhang et al respond:

Dr Evans and his colleagues have raised two main issues about our paper. The first relates to the haemodynamic significance of shunting through the ductus in our subjects. We readily acknowledge that shunting was present and that the measured left ventricular output was therefore an approximation of systemic tissue blood flow. This was unavoidable, as most babies were studied on the first day after birth, when the ductus is proceeding to close. However, on the basis of clinical assessment as well as other data not presented—for example, average left ventricular shortening fraction was 29%—we considered that myocardial dysfunction rather than ductal shunting was the most likely cause of the systemic hypotension shown.

Our study was confined to a select subgroup of babies with hypotension who failed to respond to volume loading and were thus started on inotropes. In contrast, the studies cited by Evans and colleagues were performed in groups of infants who may or may not have received volume loading and/or inotropic treatment” and in whom the level of myocardial function ranged from depressed to normal. Furthermore, most of our subjects were studied 24 hours after birth, whereas the studies cited were performed over the course of the first postnatal week. Given the substantial physiological changes in the cardiovascular system, findings obtained in the middle or end of the initial week may not necessarily be applicable to the first day after birth.

Evans and colleagues state that “left ventricular output may have increased or decreased solely because dopamine changed the volume of the ductal shunt back into the lungs”. The physiological changes we observed suggest that this was unlikely and that dopamine exerted a vasoactive effect within the systemic circulation. Thus the premise that the increase in left ventricular output was related only to greater left to right ductal shunting is not in accord with the concomitant rise in systemic blood pressure induced by dopamine. The contention that falls in left ventricular output were merely due to a reduction in ductal shunting is inconsistent with the observed fall in superior mesentric artery velocity and rise in superior mesentric vascular resistance.

A possibility deserving of consideration is that dopamine changed the degree of ductal shunting and that this comprised one component of the alteration in left ventricular output. We are not aware of any published data in newborn infants that support direct relaxation or constriction of the ductus by dopamine or of a differential effect of dopamine on the systemic and pulmonary vascular beds. Indeed, in studies performed on newborn lambs, we observed that, at infusion rates of up to 15 μg/min per kg, the systemic and pulmonary vascular effects of dopamine were proportionally similar in magnitude (J J Smolich, H Park, and D J Penny, unpublished observations). In our view therefore it was reasonable to assume that, while ductal shunting was present in our babies, the degree was not altered to a substantial extent by dopamine. However, the notion that inotropic treatment could alter ductal shunting in preterm infants has potentially important clinical ramifications and so is worth investigating.

Finally, although we agree that the illustrative example of the degree of dissociation which may occur between the level of left and right ventricular outputs is striking, examination of group data from the same laboratory suggests that, on average, left ventricular output was only 7–15% higher than right ventricular output in ventilated preterm infants. Moreover, while we did not include the data in our paper, the pulmonary trunk velocity-time integral in our infants was significantly different from the ascending aortic velocity-time integral (p < 0.9), suggesting that the marked degree of dissociation between ventricular outputs evident in the illustrative example was not a feature of the babies in our study.

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Retained umbilical artery catheter presenting as an umbilical abscess

EDITOR,—We report the delayed recognition of an umbilical artery catheter in an 18 month infant who presented with recurrent umbilical discharge. A male infant was delivered by caesarian section which was complicated by a hypoglycaemic fit. Resuscitation included the attempted insertion of an umbilical venous catheter. The line was found to be arterial and thus removed. A second attempt also entered the umbilical artery, and, as the infant was now stable, no further attempt was made.

At 15 months, the infant presented with an umbilical abscess. This was investigated after drainage to exclude a urachal remnant. An ultrasound and abdominal radiograph showed a foreign body within the common iliac artery, and, using an infraumbilical approach, part of an umbilical catheter was removed. The remnant was 10 cm in length. During the neonatal period, the umbilicus is a useful route of vascular access. The umbilical artery can be used for blood pressure and gas tension measurement but all catheters should be removed early to avoid central infection. Other complications such as thrombosis and necrotising enterocolitis have been reported.1 Migration of umbilical vein catheters into the left atrium and pulmonary veins may occur.2 Retrieval of fractured umbilical catheters during the neonatal period has been reported.1

In this case, the retained catheter was not recognised until the infant presented late with recurrent umbilical infections and illustrates a new addition to our list of differential diagnoses. The history also re-emphasises that it is essential to check central lines for completeness on removal.

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 Premedication for neonatal intubation: current practice in Australia and the United Kingdom

EDITOR,—The paper by Bhutada et al3 adds to the growing body of evidence that premedication for tracheal intubation in neonates both improves physiological stability and makes the procedure easier to perform. The results of the telephone survey of premedication use in UK neonatal units by Whyte et al2 helps to define current practice. In a similar study, we recently tried to define the routine use of premedication for tracheal intubation in term and preterm neonates in Australia and the United Kingdom, allowing comparisons to be made.

A survey was conducted of practice in Australian level 3 units (21) and UK units with six or more intensive care cots (52). The for-
be highly effective, simple to use, and rapid in action. It is also exceedingly cheap. We do not know why oral sucrose has failed to find much favour in neonatal units. Clearly neither lack of understanding of neonatal pain perception nor lack of knowledge about the analgesic properties of sucrose are significant factors. Perhaps there is an unrecognised prejudice against anything that is low tech, cheap, and not promoted by pharmaceutical companies.

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BOOK REVIEWS


After fifty years, my only real memory of the paediatrics teaching of Professor A V Neale in Bristol is the benefit to children of sunlight and the aphorism “Preconceptual and Prenatal care is crippled by a large proportion of the disadvantaged population who further disadvantage themselves by their own actions”. Regrettably this text from the USA shows us that little has changed. Over these decades the rate of prematurity, intraterine growth retardation (IUGR) and perinatal mortality has changed very little in spite of all our collective clinical efforts.

The male partner is hardly mentioned in this book so it seems that, to American eyes, the sole responsibility for producing healthy or unhealthy babies lies with the mother. All of us now know that many varied vaginal infections are associated with premature/prelabour rupture of the membranes and prematurity itself and that antibiotic treatment may have a reducing effect on these problems. Yet with a close reading of the chapter on vaginal infections, which is very well referenced, there appear to be no papers indicating that with all these infections possibly being sexually transmitted, no trials have included investigation and treatment of the male partner. For example, although Bacterial Vaginosis, Candida and Haemolytic Streptococcus are not usually recognised as sexually transmitted diseases (STD), all gynaecologists have witnessed cases where they have been the cause of recurrent vaginal infections.

Many chapters emphasise the adverse effects of alcohol, smoking, recreation drugs and poverty on the unborn fetus. I have always had a healthily sceptical interest in Jongbloet’s theory that alcohol consumption just before and at the time of conception may be responsible for a large number of chromosomal aberrations but this attractive theory is nowhere to be found in the book.

Meanwhile we are beset by new threats. A recent study, not mentioned in this book, shows ecstasy exposure being implicated in some congenital anomalies.

This is a well researched book with excellent references. Throughout, areas of research yet to be carried out are mentioned. For that reason alone it could serve as a good “ideas” source book for junior paediatricians and obstetricians to involve themselves in research projects which may one day help to reduce the continuing high incidence of potentially-damaged babies.

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Many will have experienced a feeling of being daunted when beginning a neonatal post as a doctor in training or as a neonatal nurse. The smaller the infant with which to be faced, the greater the concern over the ability to manage the infant appropriately. Levitt, Harvey and Cooke’s Practical Perinatal Care—The Baby Under 1000 Grams goes a long way to provide a very readable but authoritative book which will help prepare those in neonatal medical or nurse training to manage these infants. The book has a wide range of chapters from the practical aspects of how to put in an arterial line, perform a suprapubic aspiration of the bladder or drain a pneumothorax, to ventilation strategies, and ethical issues of the management of extremely low birth weight infants. The authors have rightly concentrated on the subgroup of neonatal patients who are less than 1000g at birth as these are undoubtedly the most challenging group, where there is the greatest mortality and morbidity, and where there is the possibility to improve the outcome with good care. Each chapter is relatively short but provides clear information from an evidence based perspective where available and is very well referenced. There is an informative chapter on iatrogenic disease which reminds the reader as to the damage which may result from the procedures and treatment given, especially if care is not taken. All chapters conclude with a highlighted box of Practical Points and there are useful diagrams and a series of black and white photographs to aid the text, although occasionally these are too small to be of real value such as in the procedures chapter. Any senior house officer, specialist registrar, or neonatal nurse starting a neonatal post would be well advised to read this useful book which will sit nicely between the several general neonatal texts that are available and the more definitive works which will remain the mainstay of neonatal reference.

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