

# PostScript

## LETTERS

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### Aspiration pneumonia in association with oral vitamin K

Most infants born in the British Isles now receive vitamin K prophylaxis, and the trend towards oral administration continues.<sup>1</sup> With the awareness that vitamin K is well absorbed from the gut<sup>2</sup> and following publication of the report linking intramuscular vitamin K and childhood cancer,<sup>3</sup> oral vitamin K prophylaxis has become more widespread. However, because of lack of uniform national policy, the practice of vitamin K administration varies from region to region. Cases of aspiration or anaphylaxis following oral vitamin K administration in neonates have not been previously reported.

We report three cases of aspiration associated with oral vitamin K, Orakay, the preparation uniformly used in Northeast England. Acute respiratory distress developed in previously well, breast fed neonates following administration of Orakay at home. All required hospital admission, and two of them had radiological evidence of aspiration.

Case 1: a 14 day old term boy was well until given a second dose of Orakay by his father. He immediately developed a cough, tachypnoea, and grunting, cried inconsolably, and refused feeds. On admission, he was apyrexial but had features of respiratory distress. A chest radiograph showed infiltration of the right perihilar and lower zones. A septic screen was normal. Two further doses of Orakay were given under hospital supervision without problems and he remained well.

Case 2: a 14 day old girl was well until the community midwife gave a second dose of Orakay. The baby coughed straight afterwards and remained very unsettled. Within an hour, she was grunting, tachypnoeic, and refusing feeds. On admission, she had features of respiratory distress. Oxygen saturation was 85% in air. A chest radiograph showed bilateral increased perihilar shadow. A septic screen was negative. She was discharged home on formula milk, and therefore did not need further Orakay.

Case 3: a 28 day old term girl was thriving and had tolerated two doses of Orakay well. When her father administered a third dose, she started to cough, became pale, unsettled,

and tachypnoeic, and refused feeds. On examination, she had features of respiratory distress. A septic screen was negative. A chest radiograph was normal. After discharge, she was given a fourth dose of Orakay under hospital supervision and remained well.

Of note, even oral administration of vitamin K can occasionally be hazardous. This is of particular concern because Orakay is not licensed in the United Kingdom. There is an urgent need to develop a consensus policy and a product that is licensed, effective, easy to administer, and has minimal adverse effect.

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### Hypothesis waiting for proof: unwrapping neonates for transfer

During transfer from the delivery suite to the neonatal intensive care unit (NICU), infants are traditionally wrapped in pre-warmed towels. Whether this is optimal remains unknown. We compared the effects on core temperature of wrapping or not wrapping neonates during their transfer from the delivery suite to the NICU.

After resuscitation, infants in both groups were transferred to a Vickers 77-transport incubator and left wrapped or unwrapped. Rectal temperature was recorded using a mercury thermometer before leaving the delivery suite and again, immediately after transfer into a NICU incubator. The study was granted ethical approval.

Our findings are summarised in the table. There were no significant demographic differences between the two groups. While the mean transfer time was longer in the unwrapped group, the mean temperature change during transit was lower although neither difference reached statistical significance. No hypothermia (rectal temperature <36°C) occurred in either group.

Wrapping infants in towels prevents convective heat gain. Additionally, leaving infants unwrapped allows essential clinical observation.

Despite the limitations of this small study, our findings challenge the practice of wrapping infants and warrant further examination in larger clinical studies.

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### Diuretics in CLD

This symposium on chronic lung disease of prematurity (CLD) by Kotecha *et al*<sup>1</sup> covered important aspects and controversies in the management of CLD. We accept the authors' inability to cover all aspects of management. We feel that some space could have been devoted to diuretics in management of CLD. Nearly all patients with CLD of some stage of their disease will receive diuretics and most of them will be on them for a long time. We came across only one systemic review by Brion *et al*<sup>2</sup> in the Cochrane database. Conclusion of the authors was that there was no beneficial effect of using distal tubular diuretics for more than 4 weeks after initial stage. There was also no benefit in adding potassium sparing diuretics or newer diuretics like metolozone. In spite of very little evidence base for diuretics in CLD, one finds nearly all CLD patients on a diuretic cocktail. In addition to their effect on electrolytes, they affect Ca/PO<sub>4</sub> metabolism. This may exacerbate osteopenia of prematurity and may have adverse effect on lung compliance. There is a need for more discussion or clear guidelines on this issue.

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**Table 1** Demographics of the two study groups and temperature difference

	Wrapped	Unwrapped
Number	10	10
Male:female	5:5	3:7
Mean weight	1.635 (kg)	1.595 (kg)
Weight range	1.29-2.35 (kg)	1.08-2.24 (kg)
Mean gestation	32/40	32/40
Gestation range	30/40-34/40	27/40-33/40
Transit time	5 min 48 sec	7 min 6 sec
Range	4-10 min	5-10 min
Temperature difference	-0.34 (°C)	-0.21 (°C)
Range	-0.7 to +0.1 (°C)	-0.5 to +0.1 (°C)

## Positioning long lines: response to Reece *et al*

Percutaneously inserted central venous lines are widely used in neonatal intensive care to administer parenteral nutrition and medications.<sup>1</sup> It is important to ascertain the position of the line tip before use as incorrectly positioned long lines can lead to life threatening complications like cardiac tamponade and pulmonary oedema.<sup>2,3</sup>

Reece *et al* suggested that it is prudent to use a routine contrast radiograph to localise the line tip in newborn infants.<sup>4</sup> We would like to comment on their suggestion and report a relevant study we carried out on our neonatal unit.

Intravenous water soluble contrast is not commonly used in neonates and very little is known about its potential side effects in premature infants.<sup>5</sup> Studies have shown that renal clearance is prolonged in premature infants because of renal immaturity.<sup>6</sup> Data in children have shown a number of possible side effects, including hypotension and cardiac arrhythmia.<sup>7</sup> Moreover, obtaining an intravenous contrast radiograph of a long line would require additional medical and nursing time as a doctor would have to "gown up" for the procedure. This may not be logistically feasible in some busy neonatal units, especially out of hours.

Reece *et al* were unable to see the line tip clearly in two cases, even after a contrast study.<sup>4</sup> This was due to delay between the injection of contrast and the radiographer exposing the film. This shows that fine coordination is required between the radiographer and the person injecting the contrast. Specific training may be necessary.

We performed a retrospective study of the reliability of plain radiographs in identifying the site of the long line tip in our tertiary neonatal intensive care unit. Over a 10 month period all 27 babies who had long lines inserted were included. In all cases an Epicutaneo-Cava-Katheter (Vygon, UK) was inserted. This is the same catheter as that used by Reece and colleagues.<sup>4</sup> Our placement aim was also similar to that in their study.<sup>4</sup>

The position of the line tip on the postinsertion x ray was independently reviewed by an experienced junior doctor (IB) and a consultant neonatal radiologist (SB). There was agreement between the two investigators in 25/27 (92.6%) cases. No complications due to line placements were observed during the study period.

We therefore feel that a plain radiograph is the safest, quickest, and cheapest way to ensure the safety of the line.

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## Neonatal sepsis in Peshawar

We wish to raise a few concerns regarding the study reported by Rahman and colleagues.<sup>1</sup>

We found it surprising that only five species of microorganisms were isolated in this series of over 1000 blood cultures obtained from neonates with sepsis. Similar studies done in other major cities of Pakistan, with much smaller sample sizes, have shown a wider spectrum of pathogens. Anwer *et al*<sup>2</sup> showed 11 species types in 109 blood cultures, Bhutta and Yusuf<sup>3</sup> showed 13 species types in 38 cultures, Khan and Akram<sup>4</sup> showed more than eight different species types from 89 cultures, and Bhutta<sup>5</sup> reported 11 species types in a series of 276 positive blood cultures. In addition to the five species causing neonatal sepsis reported by Rahman *et al* (*Escherichia coli* 36.6%, *Staphylococcus aureus* 29.5%, *Pseudomonas* 22.4%, *Klebsiella* 7.6%, and *Proteus* 3.8%), all the other investigators have also reported *Serratia spp* and *Enterococcus*, and most reported *Streptococcus pneumoniae*, *Salmonella spp*, and group B *Streptococcus*. Although the authors do not clearly state whether they excluded hospital acquired infections in their series, the studies reported by Bhutta<sup>5</sup> did exclude nosocomial infections.

The antimicrobial susceptibility data reported by Rahman *et al* are not interpretable as the number of microorganisms on which antimicrobial susceptibility testing was performed is not presented. In addition, the susceptibility results are not internally consistent; 60% of the *Staphylococcus aureus* tested are reported to be ampicillin sensitive but only 27% were Amoxicillin + Clavulanate (Augmentin) sensitive. This represents a highly unusual susceptibility result with a high percentage of *S aureus* not producing beta-lactamase enzymes to inactivate penicillin (ampicillin), but still showing resistance to a penicillin-beta-lactamase-inhibitor combination such as Augmentin. We wonder if the 60% reported sensitivity of *S aureus* to ampicillin is erroneous since the vast majority of *S aureus*, even in developing countries, are now penicillin (ampicillin) resistant.<sup>6–8</sup> We also find the 73% resistance rate of *S aureus* to amoxicillin-clavulanate (which is equivalent to methicillin resistance for *S aureus*) surprisingly high, and question if this indicates the presence of hospital acquired infections in this series.

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## Effect of head up tilting on oxygenation

We read with interest the paper by Dimitriou *et al*<sup>1</sup> in which it was confirmed again that head up tilting to 45 degrees results in better oxygenation in stable preterm neonates. However compared with our study,<sup>2</sup> in which the same effect was observed, there is a (probably) significant difference. Their infants were studied in the horizontal prone, in the horizontal supine and in the 45° head up tilt supine position whereas in our study all infants were studied in the prone position including the 45° head up tilt. We had then hypothesised that the combination of the prone position and the 45° head up tilt could facilitate diaphragmatic activity.

I do not think that this hypothesis can be totally dismissed by the results of Dimitriou *et al*<sup>1</sup> as suggested by the authors, since their infants were studied in different positions—that is, supine in their study and prone in our study.

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## Authors' reply

We thank Professor Dellagrammaticas for his comments on our study.<sup>1</sup> Dellagrammaticas *et al*<sup>2</sup> hypothesised that the combination of the prone posture and the 45 degree head up tilt position could facilitate diaphragmatic activity. We however, propose that the improvement in oxygenation seen in the head up tilt position<sup>1</sup> was more likely to be due to a change in lung volume. In the head up tilt position, the weight of the abdominal contents on the diaphragm is reduced, tending to increase functional residual capacity.<sup>3</sup> In contrast, ultrasonographic examination<sup>4</sup> has demonstrated that the diaphragm was significantly thicker at end expiratory volume in the prone rather than the supine position, which is likely to result in reduced diaphragm strength. Indeed, we demonstrated<sup>1</sup> Pimax (a measure of respiratory muscle strength) was lower in the prone compared to the supine position and the supine posture with 45° head tilt.

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### Effect of salt supplementation of newborn premature infants on neurodevelopmental outcome at 10–13 years of age

I read with interest the report by Al-Dahhan and colleagues<sup>1</sup> on the beneficial effect of NaCl supplementation of preterm infants during the neonatal period on their later neurodevelopmental outcome. They found better memory, learning, language, and educational performances at the age of 10–13 years in preterm infants who were given 4–5 mmol/day NaCl when compared with those not receiving NaCl supplement. In this regard it is relevant to mention our most recent findings describing a new aspect of the relation of neonatal sodium homeostasis to central nervous system function. Namely, we showed that hyponatraemia is one of the most significant risk factors for development of sensorineural hearing impairment detected by transient evoked otoacoustic emission and confirmed by auditory brainstem response.<sup>2</sup>

In addition, I consider their report raises an important ethical issue, in that I regard their selection of references as subjective and arbitrary. In particular, the work of our group in revealing some major features of sodium homeostasis in premature infants has been ignored; for example, renal salt wasting, sodium depletion, and hyponatraemia,<sup>3–5</sup> and the first introduction of NaCl supplementation in a dose of 3–5 mmol/kg/day to prevent

sodium deprivation, to improve somatic stability, and to avoid untoward clinical consequences.<sup>6</sup>

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#### Author's reply

Methinks Professor Sulyok doth protest too much. His early, pioneering work on electrolyte balance in the newborn is well known, and extensively cited in an earlier review of the subject co-authored by myself.<sup>1</sup> In this, *inter alia*, his study of the effect of salt supplementation on the renin-angiotensin-aldosterone system<sup>2</sup> is quoted in support of the hypothesis that hyponatraemia in premature infants is due to salt depletion rather than water retention. The reason these papers were not cited in the present paper is that they are not relevant to it. The paper is not a historical or general review of hyponatraemia in the newborn but the results of a study

specifically designed to examine neurodevelopmental outcome in two particular groups of infants previously studied by ourselves.<sup>3–5</sup> His recent study of hyponatraemia and sensorineural deafness in preterm infants<sup>6</sup> had not been published when our paper was submitted to the *Archives*, although we would certainly have referred to it if it had been.

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### CORRECTION

We would like to apologise for an error that occurred in the paper Oxygen therapy for infants with chronic lung disease by S Kotecha and J Allen (*Arch Dis Child Fetal Neonatal Ed* 2002;**87**:F11–F14). The following sentence, under the heading Weaning from home oxygen, should have read: Vermeulen *et al* showed that infants who could be weaned from oxygen had awake median saturations of 97% during one hour awake studies, spent only 14% of time with saturation  $\leq$  95% and 2% of time  $\leq$  92%.