

# PostScript

## LETTERS

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### Amiodarone and breast feeding

An infant was born at 33+2 weeks gestation by caesarean section after an in utero diagnosis of fetal ascites and tachycardia. The mother had received treatment during pregnancy with flecainide, amiodarone, and propranolol. The amiodarone was prescribed initially at 200 mg three times a day and was reduced to twice a day after 11 days.

The mother was keen to breast feed the baby. In previous reports of amiodarone and breast feeding, amiodarone treatment was for a maternal indication and hence continued post partum.<sup>1,2</sup> In this case, the amiodarone treatment stopped at delivery. However, because of the long terminal half life of amiodarone (about 50 days<sup>3</sup>), it could take several months for the level to fall. As one of the adverse effects of amiodarone is thyroid toxicity, the baby's thyroid function was assessed and found to be normal. A decision was made to allow the mother to breast feed, and the baby was closely monitored.

Breast milk was sent for analysis to determine the amiodarone level on days 5, 11, 18, and 25. It had increased on day 11 (2.1 mg/l) compared with day 5 (0.6 mg/l). This may be due to changes in composition of the milk. We do not know at what time of day the milk was expressed or whether the sample was taken at the beginning or the end of the feed. The fat content of the milk was likely to be greater after 11 days than after 5 days, which may affect the distribution of amiodarone. McKenna *et al*<sup>4</sup> described changes in amiodarone concentration in breast milk

throughout the day. By 25 days, amiodarone was undetectable. Throughout this period the baby remained well and thyroid function was normal.

Although we would not recommend that breast feeding is necessarily safe for all babies exposed to amiodarone, this case illustrates that, in some circumstances, with close monitoring, breast feeding can be initiated.

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### Reducing antibiotic use on the neonatal unit by improving communication of blood culture results: a completed audit cycle

It is common clinical practice to discontinue antibiotic treatment of asymptomatic babies if the blood cultures are negative at 48 hours.<sup>1-3</sup> However, if blood culture results are only available during the normal working day, then antibiotic treatment of some babies may continue into the next working day. In our neonatal unit, blood culture results were routinely received from the microbiology laboratory via fax as a list every morning. Extra positive results would be telephoned through, if they became available, during the normal working day. Results could also be checked by the clinical staff telephoning the laboratory during "office hours". This gave the potential for inadvertent prolongation of antibiotic courses for up to a day. In a previous study, McDonald *et al*<sup>4</sup> found this to be a common occurrence. It is of concern because unnecessary antibiotic use may contribute to antibiotic pressure within the neonatal unit and may encourage the selection of drug resistant organisms.

We performed two audits into this problem within our neonatal unit. Our audit standard

on each occasion was that antibiotics should be stopped at 48 hours, if blood cultures were negative, unless a decision to continue was clearly documented in the case notes. Babies with negative blood cultures were identified from the microbiology database. Each episode was classified into one of four groups: (a) antibiotics not started; (b) antibiotics stopped within 48 hours; (c) antibiotics given for more than 48 hours deliberately; (d) antibiotics given for more than 48 hours unintentionally. The results are summarised in table 1.

The first audit was conducted on 451 babies with negative blood cultures between January 1997 and December 1998. We were able to collect complete data from case notes and drug charts for 376 (83.4%) of these blood cultures. We found that the audit standard was not met in 144/376 (38.3%). The median (range) duration of antibiotic treatment for each baby was 60 (16.9-332) hours.

The blood culture analyser in use in our laboratory (BacT/Alert Microbial Detection System; Organon Teknika Corporation, Durham, North Carolina, USA) tests for bacterial growth every 10 minutes and communicates the blood culture status (positive or negative) to a computer. After our initial audit, we established a computer link between the blood culture analyser and the neonatal unit. This allows the clinical staff to check the status of any blood culture in the analyser in real time, 24 hours a day.

The second audit was performed on babies with negative blood cultures between May 2000 and August 2000. Two hundred negative blood cultures were identified. Complete data were available for 179/200 (89.5%). The audit standard was not met in only 20/179 (11.2%);  $p < 0.001$  compared with the first audit. The median (range) duration of treatment was reduced to 48 (1-182) hours ( $p < 0.0001$ ). There was an overall reduction of two doses of antibiotic per baby (from a mean of 8.8 to 6.8 doses per baby).

Overall, we estimated that we gave 21 684 doses of antibiotics on the neonatal unit between January 1997 and December 1998. If the computer system had been in operation during this period, we estimate that we could have reduced this by 16.2% to 18 169. We think that this magnitude of reduction in antibiotic pressure on the neonatal unit is worth achieving.

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**Table 1** Reduction in unintentional antibiotic use over 48 hours after introduction of real time availability of blood culture status by a computer link between the blood culture machine and our neonatal unit

Results	No antibiotics started	Antibiotics stopped after <48 h	Antibiotics continued for >48 h deliberately	Antibiotics continued >48 h unintentionally
First audit	25 (6.6%)	132 (35.1%)	75 (19.9%)	144 (38.3%)
Second audit	15 (8.4%)	117 (65.4%)	27 (15.1%)	20 (11.2%)

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## Swaddling and heat loss

The letter of Hawkes *et al*<sup>1</sup> raises the important issues of swaddling and temperature on admission to the neonatal unit. Besch *et al*<sup>2</sup> carried out a limited comparison of different swaddling materials and found a transparent plastic bag together with radiant heat to be effective in preventing heat loss in infants over 2 kg. Following a report in the literature,<sup>3</sup> we have begun wrapping all preterm infants < 1000 g in a thin plastic wrap. The wrap is preheated on a radiant warmer and the infant is immediately placed (undried) on the plastic sheet, which is folded over to completely (but loosely) enclose the torso and extremities from the neck down. The infant is left in the wrap until transported to the neonatal unit and the temperature has stabilised in a humidified environment. The median temperature of the 19 < 1000 g infants admitted since wrapping was commenced was 36.7°C on arrival to the nursery compared with 35.5°C for the previous 86 unwrapped infants ( $p = 0.002$ ; using Mann-Whitney U test). There were no significant differences in birth weight, gestational age or Apgar scores between the groups.

Although our experience is in smaller preterm infants (who are more prone to hypothermia), our results are in keeping with those of Vohra *et al*, who studied infants < 32 weeks.<sup>3</sup> We now plan to wrap all preterm infants < 1500 g.

The plastic wrap is likely to be more effective than towels because of reduction in evaporative heat loss and because it allows observation of the infant. However, the plastic wrap is unlikely to significantly reduce radiant heat loss, so an additional heat source is essential for preterm infants. Some form of head swaddling is also important and needs further study. Aluminum foil may reduce evaporative, convective, and radiant heat loss but does not allow observation or radiant warming.

It appears there are many aspects of swaddling that require further investigation.

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## Preventing hypothermia at birth in preterm babies: at a cost of overheating some?

In the Epicure study, the odds ratio of death before discharge for babies whose temperature on admission to the neonatal unit was > 35°C was 0.58 (95% confidence interval (CI) 0.39 to 0.85) compared with those with lower temperatures.<sup>1</sup> In 2001, we therefore introduced a policy of wrapping neonates < 30 weeks gestation in polythene bags at birth without first drying them. Temperatures on admission to the neonatal unit after the introduction of this policy were compared with those of historical controls of < 30 weeks gestation admitted unwrapped between 1996 and 2000. The admission temperatures were analysed by stepwise multiple regression against being “bagged” or not, time to admission to the unit, birth weight, gestation, mode of delivery, month of delivery, and maternal temperature. Significant coefficients of variation existed between admission temperature and:

- being bagged +0.35°C (0.09 to 0.62) (coefficient, 95% CI);
- time to admission –0.02°C (–0.01 to –0.03) per minute;
- birth weight +0.07°C (0.02 to 0.1) per 100 g;
- gestation +0.0007°C (0.0002 to 0.001) °C per week.

Thus “bagging” increased admission temperatures by 0.35°C, which is rather less than the rise of 1.9°C in babies < 28 weeks gestation reported in a previous study.<sup>2</sup>

Table 1 shows that, in the comparable groups, this rise of 0.35°C resulted in a significant reduction in incidence of hypothermia (< 35.5°C) in “bagged” babies. However, significantly more of them (12%) were hyperthermic (> 37°C), a phenomenon previously reported but not discussed.<sup>2</sup> The risks of hyperthermia are less well defined than those of hypothermia, but it may increase the risk of neurological damage, particularly after ischaemia.<sup>3</sup> The technique of wrapping babies in polythene bags would seem to benefit very preterm babies, although we may yet have to learn to use it appropriately.

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## Technique for insertion of percutaneous central venous catheters in the newborn period

The use of percutaneous central venous catheters is of proven value for the provision of parenteral nutrition and intravenous drug treatment in neonates. They have become an integral part of the management of very low birthweight infants in most intensive care units.

At the Royal Children’s Hospital in Melbourne we used a silastic catheter, which has an external diameter of 0.6 mm and comes in a variety of different lengths (Epicutaneo-cava catheter manufactured by Vygon; lengths 15, 30, and 50 cm; ref nos 2184.015, 2184.00, and 2184.005; cost AU\$59.10). It is packaged with a metal 19 GA butterfly needle for use in insertion of the line.

This technique has some drawbacks.

- (1) The 19 GA needle is difficult to put directly into neonatal veins because of its large size.
- (2) It can be difficult to appreciate “flash back” of blood into the metal needle.
- (3) It is not possible to “flush” the needle to ensure correct positioning of the line as well as patency of the vessel.
- (4) It is not feasible to place femoral venous lines using this method.

We therefore use a method whereby the vein, using the Seldinger technique, is ultimately cannulated with a 20 GA catheter through which the silastic line can be inserted.

(1) The procedure should be carried out under optimal conditions using an aseptic technique. If the infant is already ventilated, we advocate the use of a muscle relaxant as well as adequate sedation. This is especially advisable for insertion of femoral venous lines.

(2) The vein is initially cannulated with a 24 GA (external diameter 0.7 mm) cannula. The sites most often used are the great saphenous vein at the ankle or knee joint, the femoral vein, the basilic or cephalic veins in the antecubital fossa, or, occasionally, the superficial temporal vein. A transilluminator or “cold light” inserted into the finger of a sterile glove can be of use in locating deep veins as well as protecting the sterile field.

(3) A guidewire is then inserted through the cannula into the vein. We use a “duoflex spring wire guide”: diameter 0.45 mm, length 25 cm (duoflex spring wire guide manufactured by Arrow; product no AW-04018; cost

**Table 1** Incidence of hypothermia and hyperthermia in control babies and babies wrapped in polythene bags (study group)

	Control group	Study group	Difference (95% CI)
Number	230	48	–
Gestation (weeks)	27.5 (23–29)	28 (23–29)	–
Weight (g)	1020 (400–1900)	1027 (500–1700)	–
Number <35.5°C	96 (42)	12 (25)	–17 (–2 to –29)
Number >37.0°C	1 (0.4)	6 (12.5)	12 (5 to 24)

Values are either median (range) or number (%). CI, Confidence interval.

AU\$13.00; Insyte intravenous catheter manufactured by Becton Dickinson catheter; GA 24, 22, and 20; cost AU\$2.00). This has the advantage of having a soft tip at both ends of the wire and being a snug fit to the smallest catheter. Care must be taken not to advance the wire if any resistance is met.

(4) A small nick is made in the skin at the site of wire to facilitate the insertion of the larger intravenous cannulae.

(5) A 20 GA (external diameter 1.1 mm) cannula is then threaded over the wire into the vein (a 22 GA (external diameter 0.8 mm) can be used to dilate the vein before the larger cannula is inserted). This can be flushed with saline to ensure patency of the vein.

(6) The silastic catheter can then be fed up the vein through the 20 GA cannula with a pair of toothless forceps. Occasionally the silastic line coils up in the hub of the cannula. This can be overcome by cutting the cannula flush to the hub and reinserting the silastic line.

(7) The silastic catheter is placed to the required length and the other cannula is withdrawn.

(8) The silastic catheter should be placed outside the cardiac outline in accordance with new guidelines.<sup>1,3</sup> The position is always confirmed radiologically either by plain radiograph or, if necessary, by injection of radio-opaque dye. We have seen neonates with pericardial tamponade associated with malpositioned catheters, which has been well documented in the literature.<sup>1,3</sup>

We have found this method to be extremely reliable in the insertion of percutaneous venous catheters.

The use of the guidewire incurs additional costs (see above). In our experience these are partially offset by an improved success rate using the above method. We do not open the silastic catheter until the 20 GA is in place within the vein. This means that a line is not wasted if the vein cannot be cannulated.

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## Umbilical granulomas: a randomised controlled trial

The Archimedes section has previously contained a brief section on the treatment of umbilical granulomas.<sup>1</sup> We have now conducted a randomised controlled trial of the management of umbilical granulomas. The trial compared silver nitrate cauterisation with the use of alcoholic wipes at each nappy change (conservative management). The impetus for this work was a series of three burns to the anterior abdominal wall after silver nitrate cauterisation, seen in a single London hospital over a two year period.

The trial aimed to show equivalence between the two treatment modalities. On the basis of equal efficacy, we intended to change practice to conservative management. More than 40 infants were referred, but a large number of parents chose conservative management rather than randomisation. Difficulty in recruitment meant there were inadequate numbers to show statistical significance within the limited time span available.

The salient results were that two of three granulomas resolved over a three week period without cauterisation. Those infants whose granulomas did not resolve went on to treatment with cauterisation following a protocol that involved drying the area both before and after silver nitrate application, surrounding the umbilicus with white soft paraffin, and leaving the area exposed for 10 minutes after application. This resulted in resolution in all remaining cases without harm due to delay in treatment.

On the basis of this work, we suggest a change in current practice to initial conservative management followed by cauterisation only when conservative treatment fails.

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## Reference

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## Progressive ventricular dilatation (PVD) over the past 22 years

We read with interest the article of Murphy *et al*,<sup>1</sup> and it prompted us to review our own experience with progressive ventricular dilatation (PVD) over the past 22 years at the

Maine Medical Center (MMC). Since 1980, we have used a single approach to management of PVD. As noted in previous publications, we have considered the need for intervention to be rapid head growth defined as an increase in occipitofrontal circumference of 2 cm a week or more rather than relying on imaging.<sup>2,3</sup> As this degree of head growth suggests increased intracranial pressure,<sup>4</sup> we have intervened by directly draining ventricular fluid through a 21 gauge angiocath placed through the right coronal suture into the right lateral ventricle. This catheter is connected to a ventriculostomy drainage system, and drainage is continued for seven days if possible. The catheter is then removed and the decrease in head circumference and ventricular size recorded. The infant is watched for return of rapid head growth, and an angiocath is reinserted as needed. This procedure is repeated until the infant reaches about 2 kg in weight, and if rapid head growth continues, a permanent ventriculoperitoneal shunt is placed.<sup>5</sup> We do not use pharmacological treatment or repeat lumbar puncture to treat PVD.

As pointed out by Murphy *et al*, PVD sufficient to require intervention occurs almost exclusively in infants with grade 3 or 4 intraventricular haemorrhage (IVH). As expected, the very low birthweight infants with high grade IVH have a high mortality. Table 1 shows a comparison between the outcomes for grade 3–4 IVH at MMC during the 1980s and over the past five years (1997–2001 inclusive), and the data of Murphy *et al* grouped in the same way. As noted, there is little difference over time or between studies. Overall mortality for grade 3–4 IVH was 33% (26/79) for Murphy *et al*, 33% (31/94) for MMC in the 1980s, and 31% (9/29) for MMC in 1997–2001. Until grade 3–4 IVH can be eliminated, posthaemorrhagic hydrocephalus will continue to occur with high morbidity and mortality.

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**Table 1** Comparison between the outcomes for grade 3–4 intraventricular haemorrhage (IVH) in the three studies

	Murphy <i>et al</i> <sup>1</sup>	MMC 1980s <sup>3</sup>	MMC 1997–2001
Grade 3–4 IVH (% of all <1500 g)	79 (7%)	94 (6%)	29 (6%)
Death <14 days	18/79 (23%)	29/94 (30%)**	8/29 (28%)**
PVD requiring treatment	34/61 (56%)	24/65 (37%)	11/21 (52%)
VP shunt/late death (% of PVD treatment)	18/8 (26/34=76%)	12/3 (15/24=63%)	6/1 (7/11=63%)

\*Rate for all infants <35 weeks.

\*\*Rate for all deaths <30 days.

MMC, Maine Medical Center; PVD, progressive ventricular dilatation; VP, ventriculoperitoneal.

## Do we need to assess the thyroid function in the infants of mothers with Hashimoto's thyroiditis?

We read with interest the recent comprehensive review of neonatal thyroid disorders, which gave evidence-based answers to many important questions. The author recommended that all babies born to mothers with Hashimoto's thyroiditis should be reviewed at 10 days to 2 weeks and a thyroid function test taken because infants may develop transient hypothyroidism or, very rarely, hyperthyroidism.<sup>1</sup>

As paediatricians, in a hospital with a paediatric endocrine caseload similar to some tertiary centres and a subregional neonatal intensive care unit with local deliveries of 6000 per annum, we think that the potential benefits of this practice are difficult to justify. We do understand that such practice will help in identifying babies who may develop transient congenital hypothyroidism caused by maternal thyrotropin receptor blocking antibodies. However, the incidence of this form of hypothyroidism has been estimated to be 1 in 180 000 normal infants (~2 % of congenital hypothyroidism) and the majority of them will have raised thyroid stimulation hormone levels that can be detected by the current neonatal screening.<sup>2</sup> Based on a simple calculation, in a unit of our size only one baby will be detected every 30 years. We feel that there would be major disadvantages if we are to adopt the author's recommendation. Firstly, an extra hospital visit for babies and parents; secondly the need to bleed many healthy infants; and finally the potential for confusion and unnecessary anxiety. Until objective evidence emerges about the significance of subtle thyroid dysfunction in early life we feel that the current screening programme should not be extended.

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## CORRECTIONS

In the CD Review (*Arch Dis Child Fetal Neonatal Ed* 2003;**88**:F164) reviewed by C Wren, please note that the affiliation of the authors is published incorrectly. This should have read Royal Prince Alfred Hospital, Sydney. Also, the web address in the final paragraph is incomplete. The correct address is: <http://www.cs.nsw.gov.au/rpa/neonatal/default.htm>. The errors are much regretted.

The authors would like to acknowledge and apologise for an error in our article Socioeconomic status and preterm birth: New Zealand trends, 1980 to 1999. ED Craig, JMD Thomp-

son, EA Mitchell (*Arch Dis Child Fetal Neonatal Ed* 2002;**86**:F142-6).

Paragraph four in the Results section should read "Figure 2 summarises changes in preterm birth rates by Deprivation Index decile between 1980 and 1999. During this period rates rose from 5.2% to 5.9% among those living in the most deprived areas (a 13.5% increase), from 4.0 to 5.5% amongst those living in average areas (a 37.5% increase) and from 3.1% to 5.4% amongst those living in the least deprived areas (a 74.2% increase). Thus while in 1980 a marked social gradient in preterm birth existed, by 1999 this had diminished markedly." Table 2 and table 3 are amended. These errors do not significantly change the reported trends in preterm birth or the interpretation of the findings previously published.

**Table 2** Multivariate odds ratios for preterm birth by gestational age category and Deprivation Index decile; New Zealand singleton live births 1980, 1990, and 1999

Year	NZDep Index Decile	Gestational age category			
		All preterm (n=51 711) OR*	20-27 weeks (n=2697) OR**	28-33 weeks (n=12 703) OR*	34-36 weeks (n=36 311) OR*
1980	1	1.00	1.00	1.00	1.00
1980	5	1.15	1.08	1.16	1.15
1980	10	1.36	1.18	1.39	1.36
1990	1	1.30	1.31	1.21	1.33
1990	5	1.44	1.45	1.34	1.47
1990	10	1.63	1.66	1.52	1.67
1999	1	1.64	1.67	1.44	1.72
1999	5	1.76	1.91	1.53	1.84
1999	10	1.93	2.25	1.64	2.02

Multivariate analysis adjusted for gender, maternal age, parity, birth year, decile and birth year\*decile, year\*age, year\*parity, decile\*age, decile\*parity.

\*Odds ratios (OR) with reference category Deprivation Index decile 1, 1980.

\*\*Odds ratios for the 20-27 week category did not reach statistical significance.

**Table 3** The "social gradient in preterm birth"; risk of preterm birth amongst decile 10 women compared to decile 1 women (same year), New Zealand singleton live births 1980, 1990, and 1999

Year	All preterm (n=51 711) OR*	Gestational age category		
		20-27 weeks (n=2697) OR**	28-33 weeks (n=12 703) OR*	34-36 weeks (n=36 311) OR*
1980	1.36	1.18	1.39	1.36
1990	1.26	1.27	1.25	1.26
1999	1.17	1.35	1.14	1.17

Multivariate analysis adjusted for gender, maternal age, parity, birth year, decile and birth year\*decile, year\*age, year\*parity, decile\*age, decile\*parity.

\*Odds ratios (OR) for preterm birth amongst decile 10 women compared to those in decile 1 for each particular year reflects the social gradient for that year.

\*\*Odds ratios for the 20-27 week category did not reach statistical significance.