Amiodarone and breast feeding

An infant was born at 33+2 weeks gestation by cesarean section after an in utero diagnosis of fetal ascites and tachycardia. The mother had received treatment during pregnancy with flecainide, amiodarone, and propranolol. 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 breastfeed the baby. In previous reports of amiodarone and breast feeding, amiodarone treatment was for a maternal indication and hence continued post partum. In this case, the amiodarone treatment stopped at delivery. However, because of the long terminal half life of amiodarone (about 50 days), 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 breastfeed, 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 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.

References
3. Sanofi-Synthelabo. Summary of product characteristics, Cordarone X. Sanofi-Synthelabo, UK.

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. 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 found this to be a common occurrence. It is of concern because unnecessary antibiotic use may contribute to antibiotic pressure within the neonatal unit. 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 analyst 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<0.0001 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).

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 results by a computer link between the blood culture machine and our neonatal unit

<table>
<thead>
<tr>
<th>Results</th>
<th>No antibiotics started</th>
<th>Antibiotics stopped after &lt;48 h</th>
<th>Antibiotics continued for &gt;48 h deliberately</th>
<th>Antibiotics continued for &gt;48 h unintentionally</th>
</tr>
</thead>
<tbody>
<tr>
<td>First audit</td>
<td>25 (6.6%)</td>
<td>132 (35.1%)</td>
<td>75 (19.9%)</td>
<td>144 (38.3%)</td>
</tr>
<tr>
<td>Second audit</td>
<td>15 (8.4%)</td>
<td>117 (65.4%)</td>
<td>27 (15.1%)</td>
<td>20 (11.2%)</td>
</tr>
</tbody>
</table>
Swaddling and heat loss

The letter of Hawkes et al2 raises the important issues of swaddling and temperature on admission to the neonatal unit. Besch et al3 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,4 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 (but loosely) to 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) than those studied by Vohra et al, there were significant differences in birth weight, gestational age or Apgar scores between the groups.

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.2 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 hypothermic (>37°C), a phenomenon previously reported but not discussed.6 The risks of hypothermia are less well defined than those of hyperthermia, but it may increase the risk of sepsis and damage of partially asphyxiated infants.7

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.8

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References

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 parental 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 slastic catheter, which has an external diameter of 0.6 mm and comes in a variety of different lengths (Epicutanocava 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 slastic 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 “duoduo spring wire guide”: diameter 0.45 mm, length 25 cm (duoduo spring wire guide manufactured by Arrow; product no AW-04018; cost £F256 PostScript

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

<table>
<thead>
<tr>
<th>Control group</th>
<th>Study group</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>230</td>
<td>48</td>
</tr>
<tr>
<td>Gestation (weeks)</td>
<td>27.5 (23–29)</td>
<td>28 (23–29)</td>
</tr>
<tr>
<td>Weight (g)</td>
<td>1020 (400–1900)</td>
<td>1027 (500–1700)</td>
</tr>
<tr>
<td>Number &lt;35.5°C</td>
<td>96 (42)</td>
<td>12 (25)</td>
</tr>
<tr>
<td>Number ≥37°C</td>
<td>1 (0.4)</td>
<td>6 (12.5)</td>
</tr>
</tbody>
</table>

Values are either median (range) or number (%). CI, Confidence interval.
Umbilical granulomas: a randomised controlled trial

The Archimedes section has previously contained a brief section on the treatment of umbilical granulomas. 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).

(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.1 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.1,2

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 outweighed by the advantage of having a soft tip at both ends of the catheter. Care must be taken not to advance the wire if any resistance is met.

A small nick is made in the skin at the site of wire to facilitate the insertion of the larger intravenous cannula.

(4) A small nick is made in the skin at the site of the vein cannot be cannulated. We do not open the costs (see above). In our experience these are a risk factor for neonatal cardiac tamponade.

(3) The silastic catheter is inserted to the hub and reinserting the silastic line. 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.

(2) The Archimedes section has previously contained a brief section on the treatment of umbilical granulomas. 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 treatments 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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Table 1 Comparison between the outcomes for grade 3–4 intraventricular haemorrhage (IVH) in the three studies

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

*Rate for all infants <35 weeks.
**Rate for all deaths <30 days.

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

References
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.1

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.2 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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References

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.msw.gov.au/rpa/neoaternal/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 Thompson, 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 37.3% increase) and from 3.1% to 5.4% amongst those living in the least deprived areas (a 74.2% increase).”

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

<table>
<thead>
<tr>
<th>Year</th>
<th>NZDep Index Decile</th>
<th>All prem (n=2697) OR*</th>
<th>20–27 weeks (n=2697) OR**</th>
<th>28–33 weeks (n=12 703) OR*</th>
<th>34–36 weeks (n=36 311) OR*</th>
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<tr>
<td>1980</td>
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<td>1.00</td>
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</tr>
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<td>1.15</td>
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<tr>
<td>1980</td>
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<td>1.36</td>
</tr>
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<td>1999</td>
<td>5</td>
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<td>1.91</td>
<td>1.53</td>
<td>1.84</td>
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<tr>
<td>1999</td>
<td>10</td>
<td>1.93</td>
<td>2.25</td>
<td>1.64</td>
<td>2.02</td>
</tr>
</tbody>
</table>

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 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

<table>
<thead>
<tr>
<th>Year</th>
<th>All preterm (n=2697) OR*</th>
<th>20–27 weeks (n=2697) OR**</th>
<th>28–33 weeks (n=12 703) OR*</th>
<th>34–36 weeks (n=36 311) OR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>1.36</td>
<td>1.18</td>
<td>1.39</td>
<td>1.36</td>
</tr>
<tr>
<td>1990</td>
<td>1.26</td>
<td>1.27</td>
<td>1.25</td>
<td>1.26</td>
</tr>
<tr>
<td>1999</td>
<td>1.17</td>
<td>1.35</td>
<td>1.14</td>
<td>1.17</td>
</tr>
</tbody>
</table>

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.