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Arch. Dis. Child. Fetal Neonatal Ed. 2007;92:F158-F159
doi:10.1136/adc.2006.106716

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Donor breast milk for preterm infants

Banking for the future: investing in human milk

Anthony F Williams, Camilla C Kingdon, Gillian Weaver

Perspective on the paper by Boyd *et al* (see page F169)

Those caring for the newborn have long appreciated the contribution made by breast milk to short-term and long-term health. In this issue Boyd *et al*¹ report their systematic search for unbiased evidence comparing outcomes of very low birthweight babies fed donor human milk or formula. The paucity of data identified from such adequately controlled studies is remarkable, given that most very low birthweight infants cared for in the neonatal units of industrialised countries will receive formula at some point during their clinical course. Boyd *et al* nevertheless demonstrate that formula-fed very low birthweight babies are at significantly increased risk of necrotising enterocolitis (NEC) compared with those fed exclusively on breast milk. Particularly striking is the observation that the estimates of risk and associated confidence intervals were virtually identical—about a fivefold increase—in the studies cited, which were carried out on three continents. This, coupled with the observation that other indicators of feeding intolerance also occurred more frequently in those receiving formula, suggests that the increase in risk is real and not a chance finding.

Mortality related to NEC and severity of morbidity among survivors make this important. The eleventh annual report of the British Paediatric Surveillance Unit cited an incidence of 2.1/1000 neonatal unit admissions, 65% of whom weighed under 1500 g at birth.² Overall mortality was 22% but it was significantly lower in those fed human milk compared with those fed on formula (5% *v* 26%, *p*<0.05). Late morbidity among survivors was not reported but data from the USA³ suggest it is considerable.

Despite these observations many neonatal paediatricians continue to cite concerns about the use of donor breast milk when mother's own is not available. Doubts primarily relate to two things: the nutritional quality of donor milk and the possibility that a recipient infant may acquire infection. In relation to the first it is worth noting that Lucas and colleagues used dripped breast milk with an average

energy density of only 46 kcal/100 ml compared with 80 kcal/100 ml for the formula in question.⁴ In the other, much smaller, studies cited by Boyd *et al* expressed breast milk was used. Only one study distinguished between expressed breast milk from term and preterm donors.⁵ The rates of growth in the preterm group were close to those observed in the preterm formula group and faster than those of infants receiving milk from term donors, a finding attributed by the author to the compositional differences between milk from mothers delivering at or before term. Boyd *et al* unfortunately seem to have grouped these two subsets in their analysis so that the distinction is not readily apparent. A practical implication of these observations is that some concerns about the nutritional quality of pasteurised donor milk could be dealt with by the collection of expressed milk, particularly from preterm donors. Anecdotally milk banks in the UK have reported increasing success with collecting preterm donor milk. This option might be examined further when considering support for breastfeeding in neonatal units, the subject of a recent research call.⁶

As Boyd *et al* indicate, the contribution made by Lucas *et al* is distinguished by long-term follow-up of the infants recruited. Remarkably, despite large differences in early rates of growth seen in the neonatal unit, no anthropometric differences were observed at school age, even in the group fed donor breast milk or preterm formula as sole diet.⁷ Although it might be argued that short-term nutritional deficit at a critical period of growth and organ development could be associated with later functional impairment through adversely programming metabolic phenotype the data provided by Boyd *et al* do not support this hypothesis. Neither the proportions neurologically impaired nor measured indices of mental and psychomotor development differed significantly between feeding groups, contrasting with the findings of a similar study by the same workers which examined outcomes in infants fed term or

preterm formula.^{8,9} In relation to other outcomes, limited follow-up data on adolescents suggest that early feeding with donor milk is associated with a pattern of reduced cardiovascular risk.^{10,11} Whether these differences result from early energy restriction, sodium restriction or other qualitative differences between human milk and formula seems uncertain.

Where transmission of infection through donor milk is concerned, it is essential from a policy perspective to balance risk carefully against the potential benefit associated with a reduction in the risk of death from necrotising enterocolitis. Provided that milk banks are run in accordance with national and regularly updated guidance^{12,13} risk can be minimised. We are not aware of any reported instances of nosocomial or vertically transmitted infection associated with the use of donated milk collected, processed and stored using systems which follow such protocols but agree there is room for closer regulation because historically milk banks have been built from minimal resources within a few neonatal units.

As Boyd *et al* point out, important practical issues about the role of donated breast milk have been raised by a recent American pragmatic¹⁴ study in which preterm neonates were randomised to donor human milk or preterm formula when required to complement or replace mothers' own milk.¹⁵ All human milk (including donor milk) was fortified and various outcomes measured including the incidence of late-onset sepsis, NEC and rate of postnatal growth. The authors concluded that donor milk offered little advantage over preterm formula, but demographic differences between groups were apparent despite randomisation. Moreover any influence of dietary exposure must have been blunted because 21% of those infants allocated to the donor milk group were given preterm formula and results were analysed by intention to treat. These factors, coupled with the universal use of fortifier, itself implicated in late-onset sepsis and NEC,¹⁶ make it difficult to draw firm conclusions.

The need to resource milk banks makes a case for modelling the cost-effectiveness of human milk banking. In the absence of sufficient UK data the review by Boyd *et al* is promising in this respect. For example, using their estimates of the absolute risk of confirmed NEC it can be calculated that, on average, one case could be prevented for every 14 babies fed on banked human milk as opposed to preterm formula.* The cost of treating NEC is

* NNT = 1/(AR control - AR treated). Absolute rates of confirmed NEC were: sole DBM 2%; sole formula 9%—see table 3 in reference 1. NNT = 1/(9%-2%).

high, exceeding \$200 000 per survivor annually in an American study.³ It is possible that equally striking economic impact could result from a reduction in the frequency of less costly but much more commonly encountered problems mentioned by Boyd *et al.* For example, they cite data indicating that 89% of infants allocated to donor breast milk, but only 33% of those allocated to formula, tolerated full enteral feeding by two weeks of age. Even at three weeks 17% of those fed on formula were unable to tolerate full enteral feeds. This must have a considerable effect on the duration of parenteral nutrition with attendant complications and costs.

We suggest that pasteurised donor human milk is an important therapeutic resource in the care of very low birthweight infants. There are currently 17 milk banks in the UK. Audit data collected in 2005 by the United Kingdom Association for Milk Banking show that 850 women in the UK provided a total of 5000 litres of milk for pasteurisation and use on neonatal units. There has been a steady rise in use since 2000 and the use of donor milk is becoming a more established part of neonatal practice. Cost-effectiveness, safety, quality control and equity of access might be served best by the establishment of a national network without delay. Additional benefits of such a step would be sustainability of supply sufficient to resource further clinical research into the questions with which Boyd *et al.* conclude. Our current evidence base is over 20 years old and it would be particularly valuable to acquire more information about long-term cognitive attainment, growth and cardiovascular outcome in this very vulnerable

group, particularly the increasing numbers of those very immature infants in whom receipt of breast milk has been associated with higher Bayley psychomotor developmental index at 30 months.¹⁷ Finally, the role of fortification of donor breast milk and its use in other clinical situations (for example chronic diarrhoea¹⁸) could also be explored.

Arch Dis Child Fetal Neonatal Ed 2007;**92**:F158–F159.

doi: 10.1136/adc.2006.106716

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Competing interests: Gillian Weaver is chair of the charity United Kingdom Association for Milk Banking. Camilla Kingdon and Anthony Williams have been advisors to the charity. All act in an unpaid capacity.

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Neonatal transfers – a thin layer of glue to keep the service network together?

Neonatal transfers – a thin layer of glue to keep the service network together?

Gorm Greisen

Perspective on the papers by Cusack *et al* (see page F181) and Kempley *et al* (see page F185)

This issue of the Archives brings two papers on neonatal transport. The paper of Cusack *et al*¹ is of a pessimistic key. Reporting from the former Trent Health Region, with its longstanding Neonatal Survey (formerly Trent

Neonatal Survey), the authors note that the proportion of inappropriate transfers amounted to as much as 20% of all transfers, with no evidence of decline over a 10 year period. Inappropriate transfer was defined as the transfer

beyond the nearest appropriate neonatal service of a baby born in a service's district or transfer of a baby out of a tertiary neonatal service in the district where it was born. The focus in this paper is on transfers as a remedy for the lack of capacity of the stationary services—as an indicator of insufficiency.

Practising in another country, of the size of the former Trent Health Region but with its own geographical and historical peculiarities, I can comment from a different view. During a visit to Nijmegen, the Netherlands, 10 years ago, I saw my host being taken aside to help make a decision on whether to transfer a pregnant woman by helicopter to Groningen, 150 km to the north. The transfer was to be done because the neonatal intensive care unit in Nijmegen was full, the woman was to be delivered