



Highlights from this issue

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GETTING RHYTHM

Biological rhythms are fundamental aspects of biology and physiology: cellular clocks are probably as old as life itself, and the more complex the organism, the more complex and interrelated these clocks become. Biological rhythms have been well studied in non-humans and human adults. But fetuses have rhythmicity too, and there has been very little information about how human fetal rhythms transform into 'adult type' rhythms during infancy. Filling this gap, Joseph and colleagues have described the ontogeny of rhythmicity in infancy, and have shown how different 'adult' rhythms do not all happen at once, but appear in sequence: first cortisol, then melatonin and sleep rhythms, then 'adult' type circadian temperature cycles, and finally rhythmicity of a histone gene which is related to intracellular clock functions. This is not to say that there are not other rhythms that may in future be elucidated, nor do we yet know the underlying mechanism for the development of cortisol rhythmicity. But it is nevertheless a huge step forward in our understanding of infant physiology. *See page F50*

GETTING SYNCHRONISED

One of the key characteristics of rhythms that are close in frequency is their ability to entrain each other. However this is often ignored when babies are given non-invasive nasal intermittent positive pressure ventilation (nIPPV) or bi-level nCPAP (BiPAP). I have observed that babies are often given these modalities at some pre-conceived fixed rate, with no attention to entrainment of the baby's breathing rhythm, and I wonder if failure to entrain might actually do more harm than good. The alternative is to synchronise nIPPV with the baby's natural breathing pattern, which allows for the fact that from breath to breath babies have quite variable rates of breathing, so I read the crossover trial conducted by Gizzi and colleagues with great interest. The authors did not measure work of breathing, but instead set out to analyse cardio-respiratory instability as an index of the effectiveness of the different modes of support: on this basis,

the synchronised mode appeared to work best. What they did not highlight, but which I noted with interest, was that the unsynchronised nIPPV appeared to perform worse than just nasal continuous positive airway pressure, thus reinforcing my prejudice. See what you think. We have two other papers and an editorial on the same subject. *See page F17*

NATURAL HISTORY OF THE DUCT

Oh no, not the duct again, I hear you say. But in fact we really do have something new here: Rolland and colleagues report twice weekly echocardiographic observations of the natural history of duct closure in 91 very preterm babies (24–27 weeks), unmodulated by any intervention except that one—just one—had their duct ligated. In a world full of randomised trials of strategies for shutting ducts, not one of which had a genuine control arm of babies who have never had duct treatment, this observational study is highly relevant. Unfortunately it is not conclusive, as the fates of several babies transferred to other facilities were not ascertained, and it is impossible to know whether lack of ductal treatment was a factor in any of the deaths. But this study challenges much of the received wisdom about the desirability or necessity of trying to achieve closure of a patent duct, and should cause both practitioners to reflect on their pet strategies, and researchers to consider designing the randomised trial that has never yet been done. *See page F55*

MAGNESIUM SULFATE: THE ANSWER IS ALWAYS 'YES'

There is now a body of high quality evidence for the routine use of magnesium sulfate, given to mothers with incipient preterm labour, for fetal/neonatal neuroprotection. Indeed there is a strong case, where spontaneous preterm labour appears likely in a woman at less than some agreed gestation, for giving a standard package of tocolytic, betametasone, and magnesium sulfate. But there has been a lurking concern that magnesium sulfate, which in comparison to tocolytics and steroids is the new kid on the block,

might carry some undesirable effects in terms of neonatal respiratory depression or an increased need for post-delivery intervention. It is therefore welcome that the large case-control study by Weisz and colleagues (2147 cases, 3868 controls) provides reassurance that intrapartum magnesium sulfate is in fact quite safe. So if ever the neonatal team is asked the question by obstetric or midwifery colleagues 'do you want us to give magnesium?', the answer is always 'yes'. *See page F59*

THOUGHTS ON FOOD AND FEEDING

In this edition, we carry two reviews (Embleton *et al* and Maas *et al*) broadly addressing the same issues: how can we improve nutrition, particularly for the most vulnerable babies under 27 weeks, safely and effectively? And what is the metric by which we judge 'success'? As is commonly the case in matters of nutrition, readers will probably come away with fewer certainties than when they started. The most powerful underlying theme is the need for more randomised controlled trials, so that nutritional trade-offs of benefits versus harms can be properly quantified. Until then, there will continue to be significant variations in approach both at the general level (standard procedures within a service that differ from those in other services), and the personal practices of attending physicians. *See pages F72 and F76*

GOLD STANDARD OR FOOLS' GOLD?

It has become almost an article of faith that if there is a gold standard metric that can define the effectiveness of one neonatal or fetal treatment, or the non-inferiority of another, it is the 'outcome' (meaning a multidimensional developmental assessment) at two years corrected age. How refreshing therefore that Neil Marlow stands back from this paradigm that 'everybody knows', and reflects on what 2 year outcome means, what it does not mean, and how careful we should be in interpreting trials where 2 year outcome is used—especially if it is a composite outcome with death. *See page F82*