GAVISCON (Commentary)

General aspects of reflux management

Reflux from the stomach back into the oesophagus due to poor lower oesophageal sphincter tone is common, especially in young children (Campanozzi *et al.* 2009). However, even when fluid reaches the mouth ('regurgitation') it is seldom more than a nuisance even if it does retard growth for a while, as it commonly can in children with neurological impairment or cystic fibrosis. Such problems are currently 'over-medicalised' and over treated (Khoshoo *et al.,* 2007; Orenstein and McGowan, 2008).

For nearly ten years cisapride was very widely used to treat preterm babies with mild reflux. Indeed, by the time the drug was abruptly withdrawn from sale in June 2000 after the risk of arrhythmia due to QT prolongation became widely recognised, it was being given to almost half the preterm babies cared for in some centres both in the UK and in North America. Indeed its use had been quite strongly endorsed by the European Society of Pediatric Gastroenterology, Hepatology and Nutrition in 1999 (Vanderplas *et al.,* 1999) only one year before a systematic review finally appeared showing that treatment was almost completely ineffective (Augood *et al.,* 2000). In fact it took so long to get any formal trials done that the Cochrane review only appeared *after* the drug had already been withdrawn from sale in Europe and North America on commercial grounds (Bourke and Drumm, 2002). Even more tellingly the drug was still being sold and used in many other parts of the world a full five years after that. Many clinicians then started to use domperidone (q.v.), and this drug had soon become almost as popular as cisapride (Clark *et al*. 2006) even though it also lacked controlled trial evidence of efficacy (Pritchard *et al.,* 2005). Then it too was also shown to be capable of causing potentially dangerous QT prolongation (Djeddi *et al.,* 2008).

Only rarely does reflux become a 'disease' (gastro-oesophageal reflux disease or GORD) and cause overt oesophagitis. Some clinicians, in an effort not to use medication indiscriminately, have long used sustained oesophageal pH monitoring (usually over 24 hours) as a way of diagnosing 'significant' reflux, but now it is clear that multichannel intraluminal impedence monitoring provides a far more complete and logical way of detecting episodes of reflux (Loots *et al.,* 2009). Drugs, such as ranitidine (q.v.) or, if this fails, omeprazole (q.v.), which work primarily by reducing gastric acid production, can be of real value in the occasional child with genuine osophagitis (Tighe *et al.,* 2009). They have, however, been widely used to manage reflux recently in some countries (Barron *et al.,* 2007), and, in the absence of evidence of overt osophagitis, they do very little to modify the majority of the symptoms associated with reflux in most young children (Putnam 2009). Neither is there any convincing evidence that the use of prokinetic drugs such domperidone and metoclopramide (q.v.) offers any significant benefit either (Tighe *et al.,* 2009).

The current tendency to treat most preterm infants with apnoea as though they have reflux requiring medical intervention is hard to defend (Poets, 2004) although in a small minority reflux can clearly cause aspiration pneumonia. The presence of numerous lipid-laden alveolar macrophages may be suggestive, but the presence of pepsin in bronchoalveolar lavage is probably more diagnostic. Frequent regurgitation associated with fussing, crying or arching of the back, refusal to feed, and haematemesis all suggest that acid reflux is causing oesophageal damage in need of treatment. While a range of investigative techniques have been used to demonstrate and quantify serious reflux many would suggest that the most logical approach to diagnosis is a trial of treatment. Feed thickening with agents such as carob seed flour (q.v.) may reduce the number of episodes of overt reflux, but this seldom suffices on its own in children with symptoms suggestive of oesophagitis. The one group of children in whom prokinetic drugs *do* sometimes seem to be of benefit are those troubled by aspiration pneumonia because of cerebral palsy or some other severe developmental disability (Bozkurt *et al.* 1004; Pareek *et al.* 2007).

Preterm babies used to be 'gavage' fed. That is to say they had a relatively large feeding tube passed through the mouth and into the stomach each time a feed was given, but then had that tube withdrawn again afterwards. With the development of soft, fine-bore plastic tubes, which cause less irritation than the old rubber tubes, which no longer go hard and rigid if left in place for any length of time, and which only causing a modest increase in the work of breathing if inserted through the nose, this approach has now become very uncommon. There is, however, some evidence that leaving such a tube in place interferes with the working of the muscular sphincter that limits reflux of gastric content back into the oesophagus. Indeed one small study (Peter *et al.,* 2002) suggested that doing this *doubled* the number of episodes of reflux. Most of the episodes documented in this study were minor, but it is just possible that, in a pre-term baby with troublesome reflux, leaving a feeding tube permanently in place across the gastroesophageal sphincter may sometimes make serious reflux worse.

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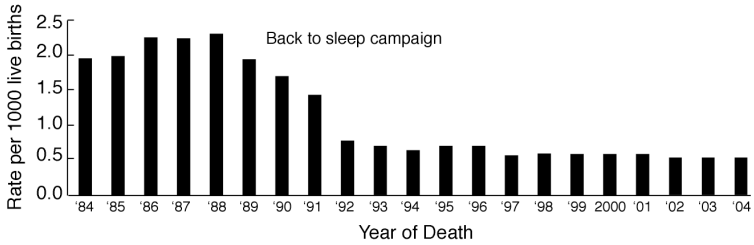
How should babies with reflux be put down to sleep ?

There is little doubt that preterm babies breathe more effectively when lying face down (supine), and that this can make a difference to the amount of oxygen getting into the arterial blood. In babies convalescing from earlier lung problems where the arterial blood is often only about 90% saturated if the baby is breathing room air a change in posture can make a significant difference to lung expansion at end expiration (Functional Residual Capacity) and resting saturation (Saiki *et al.,* 2009). While a change in posture makes little difference when saturation is already above 95%, it can have quite a marked effect when resting saturation is less than this because the haemoglobin dissociation curve starts to curve down quite sharply at this point (Quine *et al.*, 2006).

These insights have helped to place on a firmer footing the long standing practise of nursing preterm babies face down, especially if they have, or have had, respiratory problems. However we have *also* known for almost 15 years that babies put to sleep face down are much more likely to die suddenly, unexpectedly, and for no detectable reason, as those but down to sleep on their backs, and that placing a baby on its side to sleep is not a satisfactory compromise. This is particularly true in the first six months of life before most babies have learnt to roll over for themselves. The evidence is almost incontrovertible. The vigorous "Back to Sleep" campaign mounted by the Foundation for the Study of Infant Death in the UK in 1991, and its counterpart in other countries, has had a quite profound impact on cultural 'norms'. The increase in the proportion of babies put down to sleep on their backs has been paralleled by a very dramatic and welcome decline in the number of unexplained so called 'cot deaths'.



In direct conflict with this is the knowledge that small babies often 'reflux' what is in the stomach back into the oesophagus and mouth, and that a supine (face down) or left lateral (left side down) posture, (Corvaglia *et al.,* 2007; van Wijk *et al.,* 2007) combined, if necessary, with some degree of head-up tilt (Jenni *et al.,* 1997), can reduce this problem. The challenge for those nursing the preterm, or ex-preterm, baby is to know how to balance a concern for making breathing easy while also minimising reflux.

If reflux is* not *causing a problem it should almost certainly be ignored. In so far as there is any link between troublesome apnoea and troublesome reflux, the evidence is that while reflux may occur during or as a result of a period of apnoea it seldom triggers apnoea as was once thought. Self-correcting episodes of obstructive apnoea are also commoner when these babies are sleeping on their backs but such symptomless episodes are not a reason for managing preterm babies differently from term babies after discharge home from hospital (Bhat *et al.,* 2007) and, in so far as parents will instinctively tend to care for their child after discharge in the way they have seen it being cared for before discharge, this is how babies should be nursed in the pre-discharge period too. Indeed, because preterm babies are at increased risk of 'cot death', it is probably even more important that parents should be encouraged to manage *these* babies this way after discharge. Click here for a copy of the leaflet recently produced by the Foundation for the Study of Infant Death in the UK.

If reflux* is *causing a problem and resting oxygen saturation during sleep is 'low', the appropriate response should be to offer supplemental oxygen rather than recommend some other posture during sleep. What is far less clear is how low it is safe to let resting saturation go without offering extra oxygen – a move that inevitably causes parents considerable additional stress and anxiety. The first Australian BOOST trial showed that babies nursed in a way that treated fractional saturations of 91-94% as acceptable did just as well as babies in whom every effort was made to keep saturation above 95% once the baby was at least four weeks old (Askie *et al.,* 2003). However the pulse oximeters used in that trial measured *fractional* oxygen saturation, and most pulse oximeters now in clinical use measure *functional* saturation. Measurements of functional saturation are normally 1–2% higher than measurements of fractional saturation. What proportion of the babies currently being discharged home in supplemental oxygen really need such care is still, therefore, very unclear. While some gastric juices are commonly seen in the lungs at autopsy in babies suffering sudden unexpected death in infancy this is no commoner in babies left to sleep supine rather than prone, (Krous *et al.,* 2007) and seems to be an agonal event.

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