LETTERS TO THE EDITOR

Randomised trial of early tapping in neonatal post haemorrhagic ventricular dilatation: results at 30 months

EDITOR,—In reporting the results of follow up from questionnaires to the clinicians involved in the care of children randomised after the official end of this multicentre trial, Johnson et al have highlighted an important issue. Major functional loss can be identified at the age of 30 months by questionnaire, particularly when there is an unbiased comparison group. The point raised in question 3.1 was whether early tapping carried an advantage over conservative treatment in the prevention of major functional loss detectable at the age of 2 years. What may be missed, however, are impairments which, at that age, are not perceived as major deviations from the norm. Abnormalities and asymmetries of tone may escape notice in a routine examination and become obvious only at a later stage. It is therefore not surprising that there are large differences between the proportions of children reported as being ‘normal’ and those having neuromotor impairment without functional loss, in children randomised before 31 January 1987 compared with those randomised after this date.

There may also be difficulties in categorising children as multiply or singly impaired without more formal testing. Silence or poor expressivity at this age is not always attributed to shyness — particularly in the unfamiliar context of a short clinic visit.

However, for secondary questions concerning issues raised in questions 3.2 to 3.5, the sound findings and neurodevelopment at 30 months, the nature of the impairment matters. As always, the method to be used depends on what question is being asked. Further analysis of Johnson et al’s data in refining the questionnaire will succeed in identifying all the impairments which are unaccompanied by functional loss at 2 years, unless the respondents are prepared to undertakle a more detailed and structured assessment. By 4 years, it may well be possible to devise questionnaires which focus on these problems. I would strongly support their initiatives to evaluate alternative strategies for measuring health status in children.

LESLEY MUTCHE
Public Health Research Unit,
University of Glasgow G12 8RZ

Dr Elbourne et al comment:
EDITOR,—All methods of ascertainment have advantages which need to be set against their potential problems for addressing particular questions. The advantages of a questionnaire to paediatricians asking them to provide information recorded previously in clinic records were largely pragmatic: it was cheap (trial funding had ended); did not require any special investigations; nor, in the context of a randomised controlled trial, was it likely to lead to a biased comparison between the treatment groups. However, as we and Dr Much point out, the method is probably not sensitive enough to detect impairments without functional loss in 2 year old children.

One way in which the sensitivity of this approach might be improved is by prospective completion of the questionnaire by the paediatrician at the time of a routine hospital check up. This may prompt a more detailed and structured assessment. Additional questions, which cannot normally be answered retrospectively from clinic records, can also be included. For instance, in the questionnaire used in the follow up of babies entered into a multicentre trial of the use of acetazolamide and frusamide in post-haemorrhagic ventricular dilatation, information about limb and axial tone and reflex changes. This is completed by the paediatrician at the time of an outpatient clinic visit.

In this trial a randomised method for assessing groups of children will depend on the questions being addressed. In order to assess disability at particular ages, simple questionnaire may not only be sufficiently robust, but also may be the only feasible in context of follow up for large groups of geographically scattered children. The resulting increase in statistical power may more than offset the gains in accuracy which are made by using a more ‘sensitive’ test. It is these sorts of issues that we are exploring in our research assessing the advantages and disadvantages of questionnaires completed by paediatricians in clinics, health visitors, GPs and (parents and teachers for school aged children).

Pro- or antioxidant activity of vitamin C in preterm infants?

EDITOR,—It is with great interest that we read the paper by Silvers et al.1 describing plasma ascorbic acid concentrations and plasma antioxidant activity in premature infants at birth, and potential implications for reactive oxygen species induced injury. The antioxidant activity of plasma was tested by measuring the effect of plasma on lipid peroxidation in rat brain homogenate, expressed as Dmax (plasma volume in μl required for maximum inhibition of auto-oxidation). In this in vitro model, as mentioned by the authors,1 this method is not dependent on the presence of any other antioxidants. However, we are surprised that plasma samples did not show high concentrations of ascorbic acid (which contains free radicals from the drinking of hydroxyl radicals through Fenton chemistry) has a low Dmax.1 Although ascorbic acid can act as a pro-oxidant in the presence of free transition metal ions, it is a known antioxidant under other oxidative stress conditions.3 Ascorbic acid scavenges directly a variety of reactive oxygen species, including superoxide and hydroxyl radicals, suppresses the inactivation of antioxidants by oxygen generated by the myeloperoxidase-halide system, neutralises oxidants released from stimulated neutrophils in a dose dependent manner, and can regenerate membrane bound vitamin E.3,4 Ascorbic acid also has important metabolic roles — for example, in the biosynthesis of collagen, carnitine, and catecholamines.

The question, therefore, is whether in vitro observations such as the ones made by Silvers and colleagues1 are relevant to the in vivo situation. The detection of non-transferrin bound iron in plasma of preterm and term infants4 seems to support the authors’ concerns regarding a potential pro-oxidant effect of ascorbic acid in vivo. However, the various antioxidant and metabolic properties of ascorbic acid also have to be considered, and the integrated effect of high plasma ascorbic acid concentrations on the health status of premature infants is unknown. Therefore, we caution readers not to conclude that ascorbic acid is harmful to premature infants and that ascorbic acid intake needs to be restricted in these infants. Only carefully designed and performed studies of vitamin C depletion or supplementation will be able to answer these important questions.

THOMAS M BERGER
Joint Unit in Neonatology,
Hammersmith 4, Children’s Hospital,
390 Longwood Avenue
Boston MA 02115

BALZ FREI
Boston University School of Medicine,
Whitaker Cardiovascular Institute,
Room W-601,
80 East Concord Street,
Boston MA 02118
USA

Dr Powers et al comment:
There is no doubt that ascorbic acid has several important biochemical functions in the body, including, under most physiological conditions, that of antioxidant. Under the particular conditions associated with premature birth, however, which include a low plasma concentration of plasma transferrin and caeruloplasmin, and possibly the presence of non-transferring bound iron, ascorbic acid present at high concentration would be expected to act as a pro-oxidant. Our published data suggest that this is indeed the case and that high plasma vitamin C concentration at birth is associated with poor outcome. As further support for this argument we have recently demonstrated that at ratios of vitamin C:caeruloplasmin which we observe in premature babies at birth, vitamin C strongly inhibits the ferrooxidase activity of caeruloplasmin.1

We have not suggested that vitamin C per se is harmful to premature babies, but it is difficult to ignore the fact that vitamin C concentrations in infant formula are higher than those measured in human milk, and that formulas for premature babies are even more concentrated. Our data and the argument is that premature babies need high intakes of vitamin C to catabolise tyrosine completely, but our stable isotope studies of tyrosine metabolism in preterm infants suggest that this is not the case. Where there is no evidence that high vitamin C intakes are beneficial, there are indications that they may be harmful. We would therefore advocate a thorough re-evaluation of present recommendations for vitamin C intakes of preterm infants rather than a reassurance that current intakes are appropriate.

The aphorisms of Ambroise Paré

EDITOR,—Professor Peter M Dunn cited four aphorisms of Ambroise Paré which are still pertinent today.

The humanity and gentleness of Ambroise Paré, unexpected in an army surgeon of the sixteenth century, whom we would tend to imagine as a butcher, are also documented by another of his aphorisms: ‘Guérir parfait, soulager souvent, consoler toujours’ (‘To heal sometimes, to relieve often, to console always’), a relevant lesson for all medical practitioners.

J M RAMOS DE ALMEIDA
Maternity, Dr Alfredo da Costa, Rua Victora, 1000 Lisbon, Portugal

Extensive necrotising enterocolitis after a prolonged period of supraventricular tachycardia

EDITOR,—We describe a neonate who developed extensive necrotising enterocolitis (NEC) after a prolonged period of supraventricular tachycardia (SVT).

Case report

A previously healthy 24 year old mother had an uneventful pregnancy until she went into spontaneous labour at 35 weeks. A fetal ultrasound scan showed a mildly hydropic baby with ascites, an enlarged heart, and a heart rate of above 200 beats a minute.

After delivery (by emergency caesarean section) the baby was noted to be oedematous with hepatomegaly. An echocardiogram showed a structurally normal heart that was dilated and poorly functioning. Its initial ECG was consistent with an AV re-entry tachycardia. He remained in SVT despite treatment with adenosine, digoxin, propanolol, flecanide and direct current (DC) cardioversion. On day 7 he had a spontaneous and sustained reversion to sinus rhythm and an ECG indicated Wolff-Parkinson-White syndrome. On day 8 he became shocked with a distended abdomen. An abdominal x-ray picture showed free gas and at laparotomy a caecal perforation was demonstrated and resected. After initial improvement he developed Klebsiella septicaemia on day 18. He had persistent and profound thrombocytopenia and adequate antibiotic treatment failed to eradicate the organism. At laparotomy on day 26 extensive necrotising enterocolitis of his colon was found and resected. His recovery was rapid and his only subsequent episode of SVT occurred at the age of 3 months, on induction of anaesthesia for reversal of his leioseomy.

In utero SVT is increasingly being diagnosed and is well recognised as giving fetal haemodynamic compromise, which may lead to hydrops, causing a difficult delivery or even fetal death.1 Periventricular leucomalacia has also been described.2 We are not aware of any reports of NEC in a baby with utero SVT. Although the aetiology of NEC is poorly understood, poor gut perfusion is known to contribute. Decreased viscer al blood flow is not recognised as an adverse effect of inotropes or the antiarrhythmic agents used in our case. He had no other risk factors for NEC and had not been enterally fed. This baby had a prolonged period of compromise of his visceral circulation secondary to his SVT both in utero and ex utero. We suggest that this was the main causative factor for his NEC.

Catherine M CALE
Department of Immunology, Hospital for Sick Children, Great Ormond Street, London WC1N 3JH

BRIAN D SPIEDEL
Department of Neonatal Medicine, Northwest Hospital, Westbury-on-Tyn, Bristol BS15 5NB


212

Gastric motility and gastric emptying

EDITOR,—We are indebted to Kelly and Newell for the excellent summary of gastric motility.1 In their discussion of gastric motility and the measurement of gastric emptying, they state ‘a technique capable of repeated measurements of emptying of small volume feeds without disturbance of the infant in intensive care is required’. They do not mention the use of applied potential tomography (APT) — a form of electric impedance tomography (EIT). This method, which uses low electric currents, is non-invasive, and involves no radiation, provides just such a technique.2–4

In investigating preterm infants we found the APT method easy to perform, caused minimal or no upset — it need not alter the normal feeding regimen — and provided valid and reproducible results. Our results from studying 53 infants differed from those quoted by Kelly and Newell in that while there was a clear difference in gastric emptying between Dioralyte and milk, there was no difference between breast milk and formula.5 Further research suggests that the method may also be used to study gastric motility directly.

The equipment is readily available and by modern standards is quite cheap, although its use can be time consuming and requires attention to detail.

JAS DICKSON
Sheffield Childrens Hospital, Western Bank, Sheffield S10 2TH


Dr Newell and Kelly comments: We thank Dickson and Nour for their kind comments. We were aware of the use of impedance to measure gastric emptying and have previously explored its use, using a tetrapolar system. In the preterm infant, however, shifting baseline impedance thwarted attempts to measure gastric emptying. We were able, as they have been, successfully to use impedance to measure gastric emptying in infants and older children with normal and abnormal patterns.1

We are therefore delighted to hear that applied potential tomography has been used successfully to measure the gastric emptying of milk in preterm infants. It is, however, troubling that they found no difference between different milks. The more rapid emptying of breast milk compared with formula has been shown in other studies, using dye dilution,2 scintigraphy,2 and our ultrasound technique.4


