Bloodless treatment of infants with haemolytic disease

It was interesting to read an excellent review in the January 2004 edition of *Archives of Disease in Childhood* devoted to the topic of blood transfusion. At the same time the issues of haemolytic disease in the newborn (HDN) and alternatives to exchange transfusion (ET), were treated as follows: “A recent systematic review has shown that fewer infants require exchange transfusion for haemolytic disease of the newborn when high dose intravenous immunoglobulin is used.” Neonatologists generally applaud the efforts made in an attempt to achieve a “bloodless” solution to the treatment of Rh and/or AB0 HDN in a newborn whose parents are Jehovah’s Witnesses.

In 1999 we published a case of an AB0 incompatible term infant girl born to parents who were Jehovah’s Witnesses. The infant was admitted to our neonatal unit with a high serum bilirubin level necessitating ET. The parents signed a request that blood should not be administered under any circumstances. However, they authorised the use of alternative treatments: orally administered D-penicillamine (DPA) (300 mg/kg per day divided into three doses over three days), phototherapy, intravenous fluids, and recombinant human erythropoietin (200 U/kg subcutaneously on every second day for two weeks). Furthermore, we reported the outcome of this infant, who was discharged from the unit in good health following treatment. Her physical growth and motor milestones at 3 years of age revealed no red flags for neurodevelopmental maturation. In addition, the follow up audiometric tests performed on this infant were normal. To our knowledge, this was the first case of an infant who received such a combined alternative (and “bloodless”) treatment for serious AB0 HDN. As far as the mechanisms of action of DPA in HDN are concerned, it proved to be a potent inhibitor of haem oxygenase (HO), the rate limiting enzyme in haem catalysis to bile pigments, only in neonates. Therefore, this drug can moderate the postnatal formation of plasma bilirubin. The use of DPA in combination with phototherapy seems to be an appropriate combination in diminishing the intensity of hyperbilirubinemia; because DPA decreases bilirubin production simultaneously, by its antioxidant effects, DPA is able to prevent the possible adverse side effects of phototherapy that have been shown in vitro and most recently in vivo.

Another possibility in reducing the need for ET in neonates with proven HDN due to Rh and/or AB0 incompatibility, is the use of high dose intravenous immunoglobulin (HDIVIG) as was mentioned by Bolton-Maggs and Murphy. Readers will surely recognise that HDIVIG is a blood product, and is consequently unacceptable to Jehovah’s Witness families. Not only also that the costs of DPA treatment (about US$2 or €1.5 per patient) is considerably less than HDIVIG.

Although the efficacy of DPA in reducing jaundice was first shown in the 1970s, this drug does not seem to have gained acceptance in the international neonatal community. The lack of “acceptance” of DPA treatment seems sadly parochial to us, because this therapy has been used extensively in Hungary for nearly 30 years. In our own experience, more than 20 000 neonates have been treated without side effects.

The successful use of erythropoietin in the treatment of severe anaemia in a neonate, reported in our paper, should also be of considerable practical interest to your readers.

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doi: 10.1136/adc.2004.053215

Ethnic group differences in overweight and obese children with type 1 diabetes mellitus

We read with interest the paper by Saxena et al who report differences in prevalence of overweight and obesity in children of different ethnic groups.

The increased prevalence of overweight in adolescents with type 1 diabetes and among South Asian and Afro-Caribbean children with type 2 diabetes is well recognised. However, little information exists on the differences in obesity between white Caucasian and South Asian children with type 1 diabetes.

We conducted a retrospective analysis of the children with type 1 diabetes in our centre in Leicester, with an estimated proportion of South Asians in the city of Leicester of 28% (Census 2001). Our aim was to study the rates of obesity/overweight in white Caucasian and South Asian groups, and to correlate these with age, duration of diagnosis, daily insulin requirement, and HbA1c. We included children between the ages of 2 and 18 years and who had been diagnosed more than a year ago.

Data were collected for 150 children; 25% (38/150) of our study population were South Asians, with the remainder being white Caucasians. There were similar numbers of females and males represented (74 and 76 respectively).

Overall, 35% (n = 53) of children with type 1 diabetes in our centre were either overweight (>91st centile on BMI charts), or obese (>95th centile), with 18% (n = 27) of the total being obese. This compared to 23% overweight and 6% obese, respectively, in the study by Saxena et al. None of the children under the age of 4 years were overweight/obese. All the other three age groups from our service showed a higher prevalence of obesity compared to the data from Saxena et al (table 1). There was no significant difference in the proportion of overweight (19% v 16%, p = 0.61) or obesity (16% v 20%, p = 0.57) between girls and boys.

There were no statistically significant differences in the rates of overweight or obesity between white Caucasian and South Asian children at any age grouping.

Furthermore, there was no significant difference in the two subgroups in relation to age, duration of diagnosis, daily insulin requirement, and metabolic control (median HbA1c 8.4% v 8.8% respectively).

In conclusion, just as there is a worrying high and increasing level of overweight and obesity in the general population, we have confirmed that this is an even greater problem in children with diabetes than adolescents with diabetes in both our major ethnic groups. The concerns expressed by Saxena and colleagues are even greater in children with diabetes because of the adverse cardiovascular prognosis for young people with type 1 diabetes.

Table 1

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Table 1 Prevalence of obesity and overweight in children with type 1 diabetes mellitus

Factors

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1 Bolton-Maggs PHB, Murphy MF. Blood transfusion. *Arch Dis Child* 2004;89:4-7.
The management of childhood diabetes needs to focus not only on glycaemic control but also on efforts to prevent excessive weight gain and to reduce other cardiovascular risk factors.

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ESPE/LWPEC Consensus Statement on diabetic ketoacidosis in children and adolescents (Arch Dis Child 2004;89:188–94)

Given the fact that patients with type 1 diabetes have a life-long predisposition to recurrences of diabetic ketoacidosis, it is remarkable that the approach to the management of this complication is taught in a fundamentally different way in paediatrics and in adult medicine. In the former, the primary aim is to eliminate ketonaemia and ketonuria expeditiously, using a fixed dose and evidence based insulin infusion, namely, 0.1 unit/kg/h, which is maintained as long as necessary even if it entails the risk of hypoglycaemia, the latter eventually being circumvented through the infusion of intravenous glucose, given the fact that the resolution of acidaemia takes longer than the normalisation of blood glucose concentrations.

The teaching in adult medicine, conveyed through the medium of the handbook most likely to be used by junior doctors, is that normalisation of blood glucose is paramount, hence the preoccupation with a sliding scale insulin regime targeted at the blood glucose, as opposed to a fixed dose regime targeted at ketonaemia and ketonuria.

What this means is that, in the transition from childhood to adulthood, a diabetic will encounter a change in emphasis during the management of recurrences of ketoacidosis. I am not sure that this is right.

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References

Soy formulas and hypothyroidism

We were interested in a recently published article in Arch Dis Child that of Conrad and colleagues. They concluded that infants fed soy formula had a prolonged increase of thyroid stimulating hormone when compared to infants fed by non-soy formula. We have some criticisms of their study methods:

In this retrospective study there was a notable difference between the patient numbers in the soy diet group (n = 8) and non-soy diet group (n = 70). It is well known that in prospective studies in which data of two groups are compared, in order to gain statistically significant results there should be a minimum of 10 test subjects in each group and the numbers in the groups should be close. Although it is not essential to follow this rule in retrospective studies like the one of Conrad et al, the statistical reliance of the study fails since the soy diet group has eight patients whereas the other one has 70.

Secondly, in studies in which comparisons of any of body fluid parameters are made for each group, for better results, it is important that the materials must be studied in the same sessions using calibrated machines after the materials have been stored appropriately. This could not be achieved since the study was retrospective, and it is therefore inevitable that there were differences between the thyroid stimulating hormone and thyroxine results of the soy diet and non-soy diet groups. For these two reasons we think it is impossible to conclude that soy formula decreases the success of treatment in congenital hypothyroidism. We believe that further prospective controlled studies can better shed light on this topic.

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Reference

Evidence based guideline for post-seizure management

Following the publication of the guideline review “Evidence based guideline for post-seizure management in children presenting acutely to secondary care” we would like to clarify the following.

First, the guideline is published in its original algorithm format in a peer reviewed journal as well as being available on the PIER website (www.pier.shelf.ac.uk), complete with minor changes following the updated systematic review in 2002.

Second, the guideline was not published until it had been assessed with regard to ease of use and clinical impact. The findings of this large scale field study show its effectiveness in improvements in quality of care and are also published.

Third, the original guideline was developed by The Paediatric Accident & Emergency Research Group, and represents many years of work. The individuals and affiliations at the time of the research are as follows:

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Ethics: the third dimension

In essence, ethics provide the guidelines for civilised human interaction. It is an evolving concept, but through the ages some accepted ethical principles crystallised. The first crude definition focused on the individual’s responsibility towards his community, prioritising the interests of the community. However, the events preceding the French revolution and the brutality of the two world wars emphasised the need to protect individuals and minority groups against abuses of power. The ethical focus shifted from individual responsibility towards the protection of individual human rights. With the swing of the pendulum, individual rights were often protected to the detriment of the larger community.

In medicine the same shift in emphasis forced the current ethical debate on the delicate balance between the interests of the individual and that of the community, especially in resource limited settings. The reality of the third millennium is that all the world’s inhabitants are essentially part of the same global community. The two dimensional balance between the individual and the community need to reflect this global ethical responsibility.

The third millennium also confronts us with the neglected third dimension of the ethical responsibility. It is not only the interests of the individual versus that of the community that

www.archdischild.com
Splenectomy in cystic fibrosis patients

A recent article, a commentary, and two letters1,2 in Archives have revealed controversy over the place of partial splenectomy in portal hypertension in cystic fibrosis (CF). We wish to contribute to the debate with a case report:

Our male patient was homozygous for the F508 mutation. He was pancreatic insufficient, his lungs were colonised with Pseudomonas aeruginosa from an early age, and he had two episodes of allergic bronchopulmonary aspergillosis. When he was 8 years old, abdominal ultrasound showed variable echogenicity of the liver compatible with cirrhosis with thick bile in the biliary tree. Treatment with ursodeoxycholic acid was commenced. Recurrent episodes of abdominal pain associated with severe gastro-oesophageal reflux led to an anti-reflux procedure being performed when he was 9 years old. A gastrosotomy button was placed at the same time for night time supplementary feeding. Cirrhosis of the liver was confirmed intraoperatively. Over the next few years a massive splenomegaly developed. Full blood count showed features of hypersplenism but he remained asymptomatic with respect to the haematological abnormality. At the age of 13 years he developed severe abdominal pain in the area over the spleen. Oral analgesia was not sufficient to deal with this ongoing pain and he was unable to attend school. He was referred to do chest physiotherapy every two months. He had two episodes of probable melena. He developed severe, intermittent shouldertip pain secondary to dysphagic irritation from splenic infarcts. Computed tomography of the abdomen showed the spleen's span to be 30 cm, with two infarcts. Opiates were given to control pain but it proved to be intractable in an otherwise stoical patient. Eventually, because of the risk to his lungs, his poor quality of life and the risk posed to his gastrostomy by the massive spleen, partial splenectomy and possible splenorenal shunt were planned. Pneumococcal vaccine was prescribed. His white cell count (WCC) was 1.5 × 10⁹/L, platelet count 58 × 10⁹/L, and INR 1.6. At laparotomy, perisplenitis in the dia-

The alarm was raised by his school teacher who noted a large red mark on the back of his neck and shoulder for which apparently he could not give a logical explanation.

On examination, he indeed had a geographical area of redness on his skin from the back of his neck down to the right arm pit. There were drip marks. I did not get a coherent explanation for the mark from the little boy. I initially interviewed him without his parents being present on Social Services' request. However, because of the child's obvious learning difficulties I asked mum to come in towards the end of the interview and we discussed the history with her. She denied all knowledge of him having sustained an injury in the last few days.

I tried to wash off the skin mark with water and tissue, in front of the mother and the social worker, with no effect.

I therefore told mum and the social worker that I was not sure as to the origin of the mark. It did not have any characteristics of any particular injury nor was it something that could be washed off. I told them that I needed to observe him overnight to see if it evolved into anything (there was a significant amount of pressure from the social worker not to let him go home that night as well).

I documented my thoughts in the notes very clearly and never doubted that I suspected non-accidental injury.

The next morning the entire skin discoloration washed off with soap and a scrub! Mum was extremely upset with the whole situation and wanted to talk to me. She at that point disclosed that he was drinking a soft drink called "Vimto" which was quite dark red in colour. She was also upset that we had kept him in on suspicion of "abuse".

I was able to place her by reading out my documentation that clearly said that I was not sure of the origin of the mark and I could not draw any firm conclusions from it.

This just highlights the sort of pressures that can be brought to bear from various quarters on a consultant paediatrician dealing with child protection medicals. It also highlights the need for us to be vigilant about simple things which can give rise to very suspicious looking skin marks. And lastly, perhaps most importantly, it highlights the extreme importance of honest, clear, unequivocal, contemporaneous notes, as this is what stopped this situation from becoming a risk management and complaint issue.

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doi: 10.1136/adc.2004.051706

Rip peristoeal reaction: did you think about chest physical therapy?

Rib fractures are uncommon in infants. Child abuse must be suspected, especially when location is posterior, as explained by the lever phenomenon.3 The positive predictive value of rib fractures as an indicator of abuse is 95–100%.4 Bone fragility diseases, severe cough, and cardiopulmonary resuscitation can cause rib fractures, and chest physical therapy (CPT) has only been mentioned in a recent retrospective series.5

From May 2000 to May 2003 we prospectively collected chest radiographs performed as a workup for bronchiolitis, and collected six cases of infants less than 2 years old for

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doi: 10.1136/adc.2004.051508

References

1 2003;88:143–5.
3 2003;88:649.
4 2003;88:649.

doi: 10.1136/adc.2004.054106

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1 2003;88:143–5.
3 2003;88:649.
4 2003;88:649.
whom lateral rib fractures or sequela were diagnosed. With assistance from clinics, biology, radiology, and follow up, child abuse was ruled out. CPT was the only aetiology retained. It consisted in repetitive anterior cephalo-caudal compressions and provoked cough, following French national consensus. Twelve of 14 fractures were located on the lateral part of the fourth to seventh ribs, none at the costovertebral junction; physiotherapists hypothesise (unpublished data) that repeated CPT leads to subperiosteal fractures; this may relate to the hypothesis that periosteal reactions with no direct signs of is notable that 12/14 lesions consisted of sixt ribs, without any lever phenomenon. It during CPT, maximum pressure is located in anterior mid-thorax, namely the fifth and sixth ribs, without any lever phenomenon. It was ruled out. CPT was the only aetiology. We are thus thorough in assessing a non-accidental injury.

Pediatricians must consider the devastat- ing psychological effects of a wrong suspecti on of child abuse on the entire family. The benefit of CPT in bronchiolitis should be validated. To assess diagnosis, radiologists must preciely determine the location of the fractures on the chest and along the rib, and precisely describe radiological features.

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The National Health Service in Scotland: origins and ideals, 1900–1950


At the back of an old family album is a photograph of a bewhiskered gentleman posing with his wife on the steps of a grand house with a pillared portico, surrounded by his staff including the chauffeur of the Rolls Royce that was de rigueur at that level of society. He was my great-uncle, a successful practitioner in Burslem, and his financial success contrasted with that of his brother, a Glaswegian obstetrician, who lived in comfortable but by no means plushocratic style, his earning capacity restricted by time spent with indigent patients in the Duke Street and Royal Maternity Hospitals. This contrast between revered traditions and service oriented practice encapsulates the differences between the English and Scottish medical systems in the early part of the twentieth century that are explored in some detail by the author, and which he believes were largely responsible for the relatively easy transition from private to socialised medicine in Scotland.

Scotland of course had the added advantage of an earlier experiment in state provided medicine in the form of the Highlands and Islands Medical Service, and this is discussed in the first chapter of this book. However, the author points out that it had another and even greater advantage that is now all but forgotten. On the day I was born, 2 July 1936, the Report of the Committee on Scottish Health Services (the Cathcart Report) was published. It attracted little attention outside Scotland. The Times of that day, given to me as a birthday present, carried a half column summary of the report, with no editorial comment—contrasting with the two columns devoted to racing and service provision. But this report was seminal in providing a blueprint for the later NHS (Scotland) Act, which was actually written before the England and Wales Act, and which ensured that the course to state medicine in Scotland was quite different to that in England. For instance, in Scotland from the inception of the NHS the teaching hospitals were administered by the Regional Hospital Boards, and we were therefore at the centre of service provision, rather than standing aloof under a Board of Governors, a situation that would not be remedied for several decades.

This book is however much more than just a history of Scottish medicine in the first half of the twentieth century; it deals in great detail with the social and economic circumstances that led to the welcome given to the NHS by Scottish doctors. It is also justifiably critical of the failure of the BMA to comfort these feelings, undoubtedly shared by the great majority of the medical profession in Scotland.

Finally, readers may well ask why a non-paediatric book has been sent for review to the Archives. The author is in fact Dr Morrice McCract, formerly of the Royal Hospital for Sick Children in Edinburgh, and well known in paediatric gastroenterology and cystic fibrosis circles. Morrice has been miraculously transformed into a distinguished historian, and his book will appeal not only to those interested in the development of state provided medicine, but to anyone interested in the social, economic, and political history of Scotland.