properties of the anaphylatoxins.[15] Their secondary separation medium is a polyvinyl alcohol gel to which tryptophan is attached as a ligand. Tryptophan serendipitously binds preferentially to anti-acetylcholine receptor antibodies, but also activates complement. Using the serine protease inhibitor nafamostat mesilate as an anticoagulant, they were able to generate C3a but to inhibit C5a production. In so doing suppressor-inducer cells were activated, and in a series of patients with myasthenia gravis impaired suppressor T-cell function was restored.

This surprising finding casts doubt on the validity of controlled trials of plasma exchange that have incorporated a sham plasmapheresis in the control arm. In these procedures plasma is removed from the red cells in a cell separator but, without the patient's knowledge, it is then recombined with the cells before reinfusion. The risk of reinfusing anaphylatoxins and a subsequent immunomodulatory effect is apparent. In the best known of such trials,[16] which effectively ended the use of plasma exchange in rheumatoid arthritis, plasma exchange produced a striking subjective improvement as well as a stronger grip and less morning stiffness. Sham plasmapheresis produced equal benefits, which were at the time attributed to placebo effect. The possibility that sham procedures have a genuine immunomodulatory effect should now be entertained.

CHRONIC LIVER DISEASE AND HAEMOPHILIA

THESE are difficult times for haemophiliacs. Initial optimism in the early 1970s that introduction of clotting factor concentrates might restore patients to good health with a normal life expectancy has given way to an increasing appreciation of the hazards produced by the contaminants of these preparations. Human immunodeficiency virus (HIV) infected a substantial proportion of haemophiliacs between 1979 and 1985; it has now been virtually eliminated from factor concentrates but the clinical sequelae are likely to remain for many years to come. Less dramatic, but no less prevalent, has been infection with hepatitis viruses. The widespread introduction of hepatitis B virus (HBV) immunisation should eliminate HBV infection, leaving non-A, non-B virus(es) as the major problem.

Acute post-transfusion hepatitis[1] and chronic increases in liver enzyme concentrations[2] have long been associated with both factor VIII and factor IX concentrate infusion, but those caring for haemophiliacs were slow to accept chronic progressive liver disease as an important complication. Few haemophiliacs had any signs or symptoms of liver disease, deaths from hepatic failure were rarely reported, and the raised aminotransferase levels were attributed to chronic persistent hepatitis (CPH) rather than chronic active hepatitis (CAH).[3] Percutaneous liver biopsy, the hepatologist's gold standard, was seldom undertaken; not only was it believed to be unduly hazardous,[4] but also the need to provide clotting factor concentrates made it costly. Moreover, there is an inherent paradox in giving patients such concentrates to cover a procedure designed to investigate their harmful effects.

The results of early series of patients undergoing liver biopsy[5-9] were generally reassuring in that most of them showed either CPH or mild CAH, with little to suggest severe liver damage. Later reports have been more worrying. In a seven-year follow-up study, the Sheffield group documented a significant progression from CPH through CAH to cirrhosis.[10] Their cumulative figure of 35% of patients with CAH/cirrhosis was echoed by data from West Germany, where 12% of patients who had a biopsy showed cirrhosis and a further 17% CAH.[11] Similar figures are provided in a new report from Miller and colleagues in London; in this study 7 of 28 haemophiliacs were shown to have oesophageal varices by means of post-contrast computerised tomography.[12] The evidence that chronic progressive liver disease is an important complication of haemophilia treatment is therefore becoming increasingly persuasive. Furthermore, experience with other types of viral hepatitis suggests that cirrhosis and hepatocellular carcinoma may first appear decades after infection.

Given the limitations of liver biopsy, what can be done to detect these patients? Increased serum aminotransferase levels provide no guide to prognosis, and once ascites and oesophageal varices have developed the condition has reached a very advanced stage. Serum procollagen III peptide has been suggested as a marker of hepatic fibrosis,[12] but it is also an indicator of inflammation[13,14] so results have to be interpreted cautiously. Hay et al[15] have shown that serum IgG distinguishes between haemophiliacs with non-A, non-B CPH, CAH, and cirrhosis, but this finding remains to be confirmed.

Recognition of the seriousness of liver disease in haemophiliacs demands action on several fronts. Although transfusion-related liver disorders may ultimately be prevented by improved procedures for viral inactivation[16] or

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by the introduction of synthetic factor VIII, these approaches will do little for those who are already affected. Liver transplantation cures both the liver disease and the haemophilia by providing normal endothelial cells which produce factor VIII,[17] but can hardly be advocated as a routine treatment. Effective antiviral therapy administered earlier in the course of the liver disease appears to be a more attractive option, and the possibility that alpha-interferon suppresses inflammation in post-transfusion non-A, non-B hepatitis (in non-haemophiliacs) is clearly exciting.[18] But in haemophilia one has to contend with two or more hepatotropic viruses, interaction with HIV, and the continuing infusion of clotting factor concentrates and their accompanying antigenic material. Controlled trials, preferably with histological monitoring, will be needed.

COMPLICATIONS OF ANAESTHESIA IN INFANTS AND CHILDREN

In 1954, Beecher and Todd in the USA, surveying 600 000 cases, believed the anaesthesia death rate to be "disproportionately high" in the first decade of life.[1] Anaesthesia was later implicated in 17% of perioperative paediatric deaths, at a rate of 3·3 per 10 000 operations, five times that of young adults.[2] 20% of deaths due to anaesthesia occurred in the first week of life. Is the child of the 1980s any safer?

A report from France by Tiret et al suggests that he may be.[3] In 40 240 anaesthetics in children under 15 years, taken from a larger prospective series, there was only 1 death. This apparent improvement in survival seems even more remarkable when the children are removed from analysis of the full study[4]—there was 1 death or coma in every 1925 adult cases, partly or totally related to anaesthesia.

A low death rate in children is perhaps not surprising; they do not generally have the degeneration of organ function that afflicts adults and so may be better able to survive major insults. As the French study shows, a low anaesthesia death rate may mask a high rate of non-lethal complications. There were 4·3 life-threatening complications per 1000 anaesthetics in infants (age less than 1 year),[3] a rate higher than at any age up to 75 years.[4] Cardiac arrest (usually a late event in children) occurred in 1 in every 525 infants, an alarming statistic that has not improved in 25 years.[5] 70% of the complications (and the death) occurred in children assessed as "good risk" (ASA I and II[6]).

Methodological differences preclude detailed comparison with earlier works, but it is clear that the nature of the complications has not changed. Anaesthetised children die mainly from hypoventilation, myocardial depression (both usually drug-induced), airway obstruction, inhalation of vomit, and inadequate control of fluid balance. In the French children, 59% of complications were respiratory (83% of deaths in the Baltimore series[2]) and nearly one in four complications occurred in the hour following the end of surgery. Such incidents are not the inevitable consequence of anaesthesia. They often relate closely to incorrect choice or management of the anaesthetic technique (10% and 50%, respectively, of the Baltimore deaths[2]). Tiret et al detail obvious errors such as anaesthesia without a tracheal tube in the presence of a full stomach, failure to check equipment, relative overdosage of drugs, and inappropriate use of spontaneous ventilation in infants. They conclude "most of the complications seemed avoidable".

Avoidance of complications is primarily a matter of training and experience. Nevertheless, despite the known higher risks for small children, Hatch[7] suggested that only 57% of newborn babies and 30% of other children up to 3 years underwent surgery in designated centres in the UK. Most of the remainder are treated in district general hospitals or general teaching hospitals, where numbers may be insufficient to maintain proficiency or standards of equipment. It has been recommended that in each district general hospital one or two anaesthetists should take special responsibility for children[7,8] and local improvement may be made by grouping children on to specific operating lists or by dedicating a particular theatre. Such changes are difficult to carry out because they cut across traditional working practices.

Whilst there is little reason to doubt that clinical techniques (and mistakes) are similar in most developed countries, relating the French statistics to practice in the UK or elsewhere is difficult. Moreover, it is unclear whether the participating institutions were truly representative of French paediatric practice; the report unfortunately fails to indicate whether complication rates were different in specialist paediatric, general, and private hospitals. In the UK, detailed and accurate data should soon be available. The National Confidential Enquiry into Perioperative Deaths[9] in its inaugural year is looking at all deaths of children under 10 years occurring within 30 days of operation in National Health Service, armed forces, and some private hospitals; deaths are to be compared with matched survivors and independently assessed by both surgeons and anaesthetists.

An encouraging development is the increasing availability of monitoring devices such as capnographs and pulse oximeters to aid paediatric anaesthetists. Publication of guidelines by both the College[10] and the Association of Anaesthetists[11] should improve their provision and use. At last evidence is emerging to confirm the belief that they can enhance safety for children.[12]

Anaesthesia itself is not therapeutic. Although the percentage death rate may be small, each death is a 100% catastrophe for child and family. There is still room for improvement.

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