LETTERS TO THE EDITOR

Response to venepuncture for monitoring in primary schools

EDITOR,—We welcome the commentaries that followed our paper that was published in May.1 We think, however, that we need to clarify some of the points made in these commentaries to represent the views of the team members.

The last sentence of our paper can be easily misinterpreted as conveying the idea that venepuncture is ethically acceptable if the scientific merit of the question is important and the methodology of the study is sound. We hope that the readers will be convinced after reading our paper that, in the conduct of the study, we provided information that was available to the children’s parents in the study, that discomfort and the potential risks to the participants were minimal or negligible, and that parents and children were free to decide whether they wanted to participate in the study and free to withdraw from the study at any time, even after signing a consent form.

The scientific merit of the research is an important criterion to consider in addition to honest information, minimal distress to participants, and freedom to withdraw from the study at any time.

Professor Cockburn’s commentary may be interpreted as if we were challenging the Department of Health.4 We were reviewing local research ethics committees (1991)1 and the MRC document on the ethical conduct of research in children (1991).5 Neither document was available when we planned the pilot study and came to our attention after the pilot study was carried out in May 1992. In my judgment we did not contravene the MRC document because they explicitly include ‘to obtain blood specimens’ as an example of activities requiring consent with negligible risk. It is worth commenting that for a long time we were reluctant to include venepuncture as part of our nutritional monitoring system. However, as the Department of Health was keen on postnatal iron as possible, we included venepuncture for the children in the pilot study to assess the acceptability of the procedure and to learn from the experience.

We were very critical of the decision of the BPA to classify venepuncture as a low risk procedure.2 We were surprised by Professor Hull’s clarification that in experienced hands, venepuncture is a minimal risk procedure. One of our three phlebotomists had a very high rate of technical failures. We have learnt the lesson. For our main study we have made it clear to the neonatologists that they will have to spend some time training and the amount of training will be determined by the senior chief medical laboratory officer of the department of haematology with whom we are collaborating.

Armed with the results of the pilot study we submitted a protocol to include venepuncture in our main study to ethics committees in England and Scotland. We were told to find that 25 out of the 26 ethics committees approved our request; one is still processing our application. Incidentally, only one of the ethics committees queried the gift of a T-shirt as a show of appreciation to the children and most of the headteachers collaborating with our study were supportive of this element of the study.

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Octreotide treatment associated with adrenal suppression and poor feeding

EDITOR,—Octreotide, a long acting somatostatin analogue, is increasingly used to stabilise children with hyperinsulinaemia before surgery, or even in long term control of hyperinsulinaemia.1 It has few reported side effects in this group of patients.1 We write to report probable association of the use of octreotide with potentially severe adrenal suppression and with the less dangerous, but important problem of refusal of oral feeds.

Case report
A boy was born of consanguineous parents at 35 weeks’ gestation weighing 1590 g. Hypoglycaemia was noted on the first day of life with increasing glucose utilisation to >12 mg/kg/minute. Investigations on day 8 revealed low free fatty acid and branch chain amino acid, normal growth hormone, and high insulin concentrations at the time of the hypoglycaemia. A diagnosis of hyperinsulinaemia was made and neoisobiotostia (pancreatic endocrine dysregulation syndrome), was confirmed on day 90 at 95% pancreatectomy resulting in subsequent normoglycaemia at six months2 follow up.

Plasma cortisol was 56 nmol/l at the time of hypoglycaemia on day 8. The inadequate response was thought to be due to the immaturity of the infant. The large long acting somatostatin analogue, octreotide, was commenced on day 10, 4.5 mg/kg/day along with physiological replacement doses of hydrocortisone. The predose 9 am plasma cortisol concentrations remained constantly low (56, 21, 56, 42, 14 nmol/l) until the time of surgery and cessation of octreotide and then proceeded to rise to 450 nmol/l within 48 hours and remained normal subsequently.

The baby fed extremely poorly requiring naso-gastric feeds till day 60 when a trial of diazoxide was commenced and the octreotide withdrawn. The baby fed well for eight days until diazoxide related heart failure supervened and octreotide was restarted at which point naso-gastric feeds were once again required. Octreotide was withdrawn post-operatively and immediately the child again took oral feeds.

The feeding difficulties and suppressed plasma cortisol concentrations in this child seem related to octreotide treatment. Somatostatin suppresses many peptide hormones and has a well established use in neoisobiotostia, sometimes for long periods with few reported side effects.1 Its use has been explored in pituitary Cushing’s syndrome with varying success.3 4 Suppression of appetite has been reported.4 We recommend that the Committee on Safety of Medicines in one previous adult case but there have been no previous reports of hypoprotocortisolaemia.

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Aetiology of childhood leukaemia

EDITOR,—The review by Taylor on immuno-genetics and the aetiology of childhood leukaemia,5 refers to the possible role of environmental factors, including infection, on the incidence of this disease. The observation that the mortality rate due to leukaemia rose by 4%- 5% annually in Great Britain between 1911 and 1959 is cited.2 Interestingly, 1911 is the year in which the threat of tuberculous cattle to human health was formally recognised by the British Royal Commission on Tuberculosis. This led to an increased use of preventive measures, initially pasteurisation of milk and subsequently eradication of infected cattle.

Before that time, infection of children by the bovine tuberculosis bacillus (Mycobacterium bovis) was a common event but most infections resolved spontaneously and appeared to afford protection against pulmonary tuberculosis of human origin later in life. Accordingly BCG vaccine, produced from M bovis and originally given orally to neonates, was intended to mimic this natural milk borne infection.

Some authors have claimed that BCG vaccination leads to a reduction in the incidence of leukaemias and other childhood cancers though others refute these claims. A re-evaluation of these reports revealed that BCG showed a significant protective effect only when it was given neonally and in regions where protection against tuberculosis was also demonstrable.3 One explanation of this claimed effect is that BCG vaccination enhances the ability of cell mediated immune response and prevents remissions from which cancers might otherwise arise.4 It is therefore possible that natural infection by M bovis or its artificial analogue, BCG vaccination, in infancy might afford protection against leukaemia. This hypothesis could be tested in regions or countries that are undergoing changes in BCG vaccination policies.

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