LETTERS TO THE EDITOR

Gut blood flow velocities in the newborn: effects of parent ductus arteriosus and parenteral indomethacin

Sir,-Skinner et al.1 seem to suggest that the rapid fall in blood flow velocity seen in the cerebral,2 renal,3 and mesenteric,4 arteries after an intravenous bolus of indomethacin is due to rapid closure of the ductus arteriosus and a simultaneous fall in cardiac output. Is their explanation for the recovery of regional blood flow velocities after the acute fall a gradual reopening of the ductus with increasing output?

There are several reasons why we believe the rapid fall in mesenteric blood flow velocity reflects a regional vascular constriction rather than a fall in cardiac output. Our data indicate clearly that the coeliac axis and superior mesenteric artery do not behave in the same way, a reflection of the very different vascular beds which they supply. The fall in peak systolic velocity in the coeliac axis was significantly less than in the superior mesenteric artery (p<0.034). Moreover, our child with Falot's tetralogy, who did not have retrograde diastolic flow and was inadvertently treated with indomethacin, showed no change in clinical state, yet showed the expected fall in coeliac and superior mesenteric artery blood flow velocity.

Bolus indomethacin results in a rapid increase in systolic blood pressure which parallels the changes in regional blood flow velocity representing, we believe, considerable peripheral vasoconstriction.3,5 This is hard to equate with the suggestion of Skinner et al. of a rapid fall in cardiac output, especially when data from Saliba et al demonstrate very clearly that ligation, as opposed to the treatment of the ductus with indomethacin, does not affect systolic blood pressure, but does produce a rapid increase in diastolic pressure and immediate return of forward diastolic flow velocities.6

There is no doubt that indomethacin does affect the ductus and that left ventricular output decreases with ductal closure. The question, however, is how to interpret the observed changes in regional blood flow velocity. We would suggest that ductal closure is represented by the return of forward end diastolic flow velocities which appears to be a good predictor of eventual ductal closure and that the rapid fall in velocity represents a local vasoconstriction which can be avoided by the slow administration of indomethacin which is equally effective at closing the ductus.

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Changes in body composition and energy expenditure after six weeks' growth hormone treatment

Sir,-It was gratifying to read the well controlled study by Dr Gregory and colleagues, documenting impressive changes in body composition and energy expenditure after only six weeks of treatment with biosynthetic growth hormone (hGH).1 Niccolaidis and Even in 1986 introduced the term 'leptogenic' (from the Greek word leptos=lean) to describe pharmacological agents that reduce body fat by the following means: (i) affecting appetite/satiety mechanism, (ii) altering metabolism, (iii) adjusting set point controls, and (iv) through other peripheral/central nervous system effects. Research by ourselves and others (Riten from Karolinska Institute, Stockholm, Kish and colleagues from the David College of Medicine, Houston, and Saenger and colleagues from Albert Einstein College of Medicine in the Bronx, New York) presented at the International Congress on Prader-Willi syndrome in the Netherlands in May, 1991, has documented that changes in body stature associated with the administration of growth hormone to children with Prader-Willi syndrome are often accompanied by reductions in percentage of body fat. In light of the observation reported by Forbes that children with Prader-Willi syndrome show strikingly less lean body mass than equally overweight children with exogenous obesity and the demonstration by Hill et al and Scholler et al that energy expenditure is also considerably reduced in Prader-Willi syndrome, the findings by Gregory et al suggest that hGH exerts its leptogenic effects by increasing the metabolic activity of the fat free mass.

Analysing the cases reported by Gregory et al that showed a decrease in resting energy expenditure expressed as a percentage of total fat free mass suggests that additional research might be helpful in predicting who might show a leptogenic effect to hGH treatment. Responders had normal percent static stature or isolated growth hormone deficiency. Child- ren with acute lymphoblastic leukaemia or carcinopharyngioma showed reduced metabolic activity.

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Indwelling cannula for insulin administration in diabetes mellitus

Sir,—I read with interest the study on the use of indwelling canulas for insulin administration1 and would like to report different experiences with the same device in diabetic subjects.

During summer camps in Austria in 1989, 49 diabetic subjects (aged 9-22 years) used the indwelling cannula (Insulfon, Viggo) in an open trial to test the acceptance of this device in those who inject themselves. The proposed indwelling time was 144 hours for each cannula. All the subjects were used to giving their injections themselves, most had two daily insulin injections, and about a quarter used insulin pens for multiple injections. The first insertion of the cannula was done by a doctor, afterwards the subjects were allowed to insert it themselves for summer supervision. The cannula was carefully dried before insertion; insertion sites were the abdominal wall or thigh.

Fifteen subjects used the cannula only once, 13 twice, 15 three times, four times, and one six times. The mean indwelling time was only 41.5 hours (range 1-120 hours), which is much shorter than in the British1 or Swedish study.2 Reasons for removal or change of the cannula were: loss during sports (21%), spontaneous loss (21.6%), pain at the insertion site (14.2%), and local inflammation (10.7%). In 37 cases natural history of the cannula insertion point was performed, and in 15 cases an additional recess epidemidis was found. No obvious changes in metabolic control could be observed during the use of the indwelling cannula. After the summer camp only four subjects (8%) wanted to continue to use the device.

Because of the failure of the adhesive patch the indwelling time in these subjects was only 35% of the proposed time. Therefore the major advantage of the device in reducing the number of injections was lost. Whether the Austrian climate, with higher average summer temperatures and increased sweating during normal sports, contributes to the high percentage of spontaneous losses is unclear. It is interesting, however, that the studies reporting longer indwelling times for the cannulas came from northern Europe.

In conclusion, it is my opinion that an indwelling cannula (at least in the available form) is of no advantage compared with conventional injections. Relatively high costs and the possibly increased risk of local infections must also be taken into account.

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1 Long AM, Hughes J. Indwelling cannula for...

Professor Hughes and Dr Long comment: We were interested to read of Dr Schober’s experience of using the Insulin cannula in 49 young diabetics. The circumstances in which he used the device were entirely different to those operating during our study. The comparison is therefore not a valid one and other than to comment that the device did not appear to be either effective or acceptable when tried out in a summer diabetic camp setting. We did have problems ourselves until we learned how to apply consistently the adhesive patch, such that our diabetic children were then able to participate in a wide range of activities.

We re-emphasise the value of this type of indwelling cannula device for the administration of insulin to newly diagnosed diabetics and for those children with needle phobia. Clearly, further studies are required to determine whether such a device would be of practical benefit in a wider range of circumstances.

γδ T cells in human breast milk

Sir.—We previously reported that the proportion of lymphocytes bearing the γδ T cell receptor is significantly higher in human colostrum than in either autologous or heterologous blood samples.1 Additional studies revealed that the great majority of colostral γδ T cells react with a monoclonal antibody (TC51) which recognises actively motile cells that express non-covalently bound γδ chains.2 To characterise further the phenotype of this small, but numerically important, T cell subset, we have now examined eight milk lymphocyte suspensions with a more complete panel of monoclonal antibodies directed against γδ T cell related antigens.

Direct and indirect immunofluorescence staining techniques followed by two colour cytofluorimetric analyses showed that only a few (15-35%) milk γδ T cells (TCR δ+) were CD8+, whereas nearly all were CD4+, CD5-, and CD7-. In contrast, an overwhelming preponderance (95-99%) of colostral γδ T cells displayed the HML-1 phenotype. This is the reverse of situation encountered in the bloodstream, where HML-1+ T lymphocytes are virtually absent.

Although the origin of colostral T cells is still a matter of conjecture, the fact that the phenotypic pattern of milk γδ T lymphocytes is similar, if not identical, to that of the intestinal intraepithelial counterpart suggests that these cells might originate in the gut associated lymphoid system and home to the mammary gland late in pregnancy and throughout lactation. This selective homing process by immune system cells has been well documented in experimental animal models.3

γδ T cell related lymphoid cells appear to be either effective or acceptable for use in human breast milk. Arch Dis Child 1990;65:1274-5.

2 Bertotto A, Gerli R, Castellucci G, Scalise F, Vaccaro R. Human milk lymphocytes bearing the γδ T-cell receptor are mostly δ TCS1-positive cells. Immunology (in press).

Segmental colonic transit time in Duchenne muscular dystrophy

Sir,—We read with interest the recent paper by Korman et al concerning the oroocael transit time in Duchenne muscular dystrophy.1 In contrast to reports of gastric hypomotility and intestinal pseudo-obstruction, the authors found a normal oroocael transit time. Therefore the genesis of patient’s constipation is not due to impaired small bowel motility. Colonic motility had not yet been studied in Duchenne muscular dystrophy.

For this reason, we recently studied segmental colonic transit time in 12 patients, aged 8 to 18 years (mean 12-3 years). Eight of them were confined to a wheelchair. Gastrointestinal symptoms were noted and segmental colonic transit time was performed according to a method previously described:2 20 markers were given at breakfast time to the patients for three consecutive days and plain film of the abdomen was taken at the fourth and seventh days. Ten children had at least one criteria of constipation: less than three stools per week (n=5), difficulties in defecation (n=7), and hard stools (n=3). Ten had gastrointestinal symptoms: abdominal pain (n=7) protoclic abnormalities (n=5), enuresis (n=2), and abdominal distension (n=2). Results of segmental colonic transit time are reported in the table. Seven of 12 children with Duchenne muscular dystrophy had an abnormal colonic transit time: three had stagnation at markers in the rectosigmoid area and four had an abnormal oroocael transit time in all the colon segments. No relationship was found between colonic transit time and either gastrointestinal manifestations or gravity of muscular dystrophy.

Our results show that impairment of colonic transit time is frequent in Duchenne muscular dystrophy. Immobility, weakness of abdominal wall muscles and smooth muscle involvement of the colon3 might explain the high frequency of constipation in these patients.

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Surfactant treatment for premature babies—a review of clinical trials

Sir,—In the review article on surfactant treatment,1 Survanta (Abbott Laboratories) is described as a frozen aqueous suspension. The current formulation of Survanta, recently approved for commercial use in the United States, is a suspension requiring refrigeration only. Before administration, Survanta vials are warmed to room temperature.

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Pediatric Laboratory Medicine Fund of the Royal College of Pathologists

Sir,—Funds have been made available to promote scientific interchange in all branches of paediatric laboratory medicine in the UK.

Segmental colonic transit time in 12 patients with Duchenne muscular dystrophy

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Right colon* (hours)</th>
<th>Left colon* (hours)</th>
<th>Rectosigmoid* (hours)</th>
<th>Total* (hours)</th>
<th>Constipation</th>
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*Upper limits of normal range of colonic transit time in French children are right colon, ⩽18 hours; left colon, ⩽20 hours; rectosigmoid, ⩽34 hours; and total, ⩽62 hours. Abnormal values underlined. + and − signs indicate present or absent.