LETTERS TO THE EDITOR

Gut blood flow velocities in the newborn: effects of patent 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 vasoconstriction 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 Fallot'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 blood 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.

R C COOMBS
M E I MORGAN
G M DURBIN
I W BOOTH
A S McNEISH
Institute of Child Health,
The Nuffield Building,
Francis Road,
Birmingham B16 8ET

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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 Nicolaidis 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 (Ritzen from Karolinska Institute, Stockholm, Klish and colleagues from the Baylor 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 obesity² and the demonstrations by Hill *et al*³ and Schoeller *et al*⁴ 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 variant short stature or isolated growth hormone deficiency. Children with acute lymphoblastic leukaemia or craniopharyngioma showed reduced metabolic activity.

AIPFADT
New York State
Institute for Basic Research in
Developmental Disabilities,
1050 Forest Hill Road,
Staten Island,
New York 10314-6399, USA

MORIS ANGULO
Director, Genetics,
Winthrop-University Hospital,
222 Station Plaza North,
Suite 611, Mineola,
New York 11501, USA

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Indwelling cannula for insulin administration in diabetes mellitus

SIR,—I read with interest the study on the use of indwelling cannulas 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 (Insufion, 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 doses, 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 under supervision. The skin 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, five 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 (21.4%), spontaneous loss (21.6%), pain at the insertion site dependent of injection (14.2%), and local inflammation (10.7%). In 34 cases a bacteriological culture of the cannula insertion point was performed and in 15 (44.1%) *Staphylococcus epidermidis* 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 (8.2%) 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.^{1,2}

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.

E SCHÖBER
University Children's Hospital,
Währinger Gürtel 18-20,
A-1090 Vienna, Austria

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