Correspondence

Congenital dislocation of the hip and short maternal stature

Sir,

We were interested to read the paper by Amitai *et al.*¹ reporting an association between congenital dislocation of the hip (CDH) and short maternal stature, based on a study of 33 consecutive cases and 54 controls ($P < 0.01$). We have been interested in the aetiology of CDH for many years and have just completed a study of 455 infants with CDH born in the care of the university service in Bristol, so it was easy to scan our records to find out if our data supported this new observation.

Among the 455 infants with CDH born between 1970 and 1979 all but 10 cases were diagnosed in the neonatal period. Maternal height was available in 330 cases. We took as our controls randomly selected mothers of babies born in our hospital during the same period who did not have CDH. The maternal height of the two groups was then compared, first in 5-cm subgroups and then as in the Figure below; there was clearly no statistical difference between the two groups. We conclude that whatever may be the case in Israel, in Britain short maternal stature does not appear to be associated with CDH.

We thank the Van Neste Foundation for support.

Figure Distribution of maternal height in association with 330 infants with congenital dislocation of the hip and controls, born in Bristol, 1970-79.

Reference

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Necrotising enterocolitis in the very low birthweight infant

Sir,

Drayton *et al.*¹ were so anxious to criticise our paper² that they did not read it properly. All the 'missing' figures concerning the incidence of necrotising enterocolitis (NEC) in preterm infants with birthweight above 1500 g were given in the results section.³

Regarding the age of onset of NEC and the duration of parenteral feeding recommended by us, in Wilson's series⁴ of 148 cases of NEC, 86 of whom were VLBW infants, the median age at onset was 7 days. Average age at onset in Kliegman's⁵ 123 NEC patients (70% VLBW infants) was 12 days. It is true that the age at onset of NEC has an inverse relationship to the gestational age. This is the reason for our recommendation of at least a 3-weeks period of parenteral nutrition in infants weighing 1000 g and below at birth. If our colleagues from the Southmead Health District wish to carry on with parenteral nutrition beyond this period, all we do can is congratulate them.

Drayton *et al.* are concerned about biochemical and technical difficulties. During the last 3 years we have not noted any serious adverse effect which could be attributed to parenteral nutrition (nearly 300 infants), and we feel we have avoided many cases of NEC. We think this achievement is much more important than a possible theoretical gain—such as induction of gut hormone production by enteral feeding.

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⁴ Wilson R, Kanto W P, Jr, McCarthy B J, *et al.* Age at onset of necrotizing enterocolitis: an epidemiologic analysis. *Pediatr Res* 1982; **16**: 82-4.

⁵ Kliegman R M, Fanaroff A A. Neonatal necrotising enterocolitis: a nine-year experience. I. Epidemiology and uncommon observations. *Am J Dis Child* 1981; **135**: 603-7.

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Systemic candidiasis

Sir,

Systemic candidiasis occurs particularly at the extremes of life and in the immuno-compromised host. Unfortunately the drugs currently available often have side effects that limit their use and most must be administered by the intravenous route necessitating admission to hospital. Ketoconazole is an imidazole derivative with a wide spectrum of action against pathogenic fungi. It is effective if taken orally in the treatment of chronic mucocutaneous candidiasis.¹ We have recently used oral ketoconazole in the treatment of systemic candidiasis in a neonate.

After premature onset of labour a 650-g boy was delivered by caesarean section at 28 weeks' gestation. He developed hyaline membrane disease and required intermittent positive pressure ventilation from birth until day 11. On day 21 he developed symptoms and signs of necrotising enterocolitis. Oral feeds were stopped and a 10-day course of antibiotics (ampicillin, metronidazole, gentamicin) was given. No organisms were isolated on any cultures. Normal feeds were reintroduced without any problem 2 weeks later. Progress was then satisfactory until his 64th day when his condition deteriorated. After a septic screen, he was started on ceftazidime (100 mg/kg a day). Two days later a left inguinal hernia was found which required surgical reduction after which his condition remained poor, his abdomen becoming distended with ascitic fluid. Culture of the ascitic fluid and his 64th day blood culture grew *Candida albicans*, sensitive to amphotericin B, flucytosine, miconazole, and ketoconazole. He was started on oral ketoconazole, 3.5 mg once daily, equivalent to an adult dose of 200 mg daily, because of his deteriorating condition and positive cultures. On this regimen there was a gradual improvement in his condition. There were no local or systemic side effects during treatment. Treatment was continued for a total of 10 weeks. Cultures once treatment was stopped were sterile. On day 119 he was discharged home weighing 2.52 kg. He is now 6 months old and his progress has been satisfactory.

Studies indicate that ketoconazole is a safe drug with low toxicity.² Reversible liver toxicity, manifested by mild acute hepatitis, has been reported.¹ We did not experience this problem in our patient. Alternative forms of treatment of systemic candidiasis have a greater incidence of toxic side effects and must be given by the intravenous route. The use of amphotericin B is limited

by its nephrotoxicity and flucytosine may cause bone marrow depression. Miconazole has been reported to cause superficial thrombophlebitis at the site of intravenous administration and ventricular tachycardia.³ Rarer cases of cardiorespiratory arrest have also been documented with its use.⁴

The response of our patient to ketoconazole indicates that it is an effective agent in the treatment of systemic candidiasis. It has the advantage of being well absorbed when given orally. Thus one is not faced with the problem of long-term intravenous therapy, a feature of particular importance in the neonate.

References

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Electronmicroscopy in 'absence' of islets of Langerhans in a newborn infant

Sir,

In a previous report¹ we described the case history and histology at necropsy of a boy with congenital diabetes mellitus who died on the third day of life. His brother had died 8 years previously after a remarkably similar neonatal illness, but with no diagnosis established. Our patient weighed only 2.13 kg at term, was obviously wasted, and developed respiratory distress, although the chest x-ray film was normal. Blood gas analysis indicated a mild metabolic acidosis which increased during the next 24 hours despite administration of sodium bicarbonate. The urine contained large amounts of glucose and acetone, and the blood sugar at 36 hours was > 22 mmol/l. Despite intravenous fluids and insulin, he died suddenly from pulmonary haemorrhage at age 40 hours.

Studies at necropsy showed that the pancreas was externally normal but no recognisable islets of Langerhans could be found. There were a few lymphoid aggregates and occasional granular cells which might have been of endocrine origin, but these gave a negative staining reaction for α - and β -cells. Small amounts of insulin (54 IU/g) could be measured in the pancreatic tissue, and were probably derived from the insulin given before death (the concentration in the pancreas of 2 'control' infants exceeded 2000 IU/g in each case). Immunocytochemistry and electron microscopical examination, prompted by comments after the publication