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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.

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

Sir,

In a previous report[1] 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