volume in one second (FEV_1 in ml, Pulmonet, Physiosystem), peak expiratory flow rate (PEFR in l/min, mini Wright), heart rate (pulses/min). Results as mean (SD) were compared by analysis of variance. The two groups (11 in each) did not significantly differ in age (Nebuhaler: 8·5 years, range 4·5–13 and Turbuhaler: 10 years, range 6–14). There was no difference between the baselines for any variables. Results in efficacy are presented in the table. Both treatments were effective at 15 minutes to improve lung function compared with baseline ($p<0·01$ for all variables) with little further improvement at 30 minutes. No difference between treatments could be demonstrated at any time for these variables. No cardiovascular effect was observed in the Nebuhaler group. In the Turbuhaler group, a slight increase in heart rate (median:80 to 86 pulses/min) was observed.

In conclusion, inhalation of terbutaline via Turbuhaler gave similar increase in lung function as a metered dose inhaler plus Nebuhaler in children above the age of 5 years with moderately acute exacerbation of asthma. The Turbuhaler is easy to use and to carry and can be recommended for paediatric use.

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Evaluation of a pen injector system for growth hormone treatment

SIR,—We agree with many of the comments of Gluckman and Cutfield about convenience and compliance using a pen injector system (0·5 unit increments up to a maximum of 4·0 units per injection) and the important role of a nurse educator.[1] The authors have demonstrated that if convenient doses of growth hormone using a pen injection system are administered, such as 2 or 4 units (which by serendipity fit the 0·5 unit increments and divide into 16 with no residual) then indeed this pen system is accurate and efficient. However the authors have convincingly argued that traditional fixed dose regimens of 4 units three times a week are obsolete and that the dose of growth hormone should be related to the patient's size. If the dose schedule of growth hormone is related to either weight or surface area, then usually the resulting dose will not be convenient using this pen injector system, which may lead to wastage of growth hormone at the end of the cartridge vial. After four growth hormone injections of 3·5 units, what happens to the 2 units remaining in the cartridge vial?

Dosage for small children may prove difficult, because of 0·5 units per increment dose selection. For example, a child of 0·6 m^2 treated with a physiological replacement regimen of 15 units/m^2/week as a daily injection, will necessitate large steps in dose schedule. The difference between 1·0 and 1·5 units per injection is the equivalent of dosages of 11·5 and 17·5 units/m^2/week respectively, which makes an accurate dose schedule impossible to administer. Of course, there remains the possibility of having varying doses on different days of the week, but this would probably be counterproductive for both convenience and compliance. Although the optimum dose regimen for growth hormone administered during the pubertal growth spurt is unknown, many authors have recommended an increase in dose.[2] The limitation of this pen system to a maximum of 4 units per injection makes a daily regimen of 20 or 30 units/m^2/week difficult to achieve in pubertal children. In a similar fashion, pharmacological doses of growth hormone using such a pen system for girls with Turner's syndrome will have severe limitations; because of the restriction of maximum dose, a schedule of 30 units/m^2/week will restrict the use of this pen system to a child of less than 0·93 m^2 surface area.

We agree that pen injection systems are a considerable advance in convenience to patients. However, if optimum treatment regimens are prescribed, these should not be introduced in a system with inflexible dose selection which may be detrimental to accurate dose schedules and potentially wasteful of expensive resources.

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Dr Cutfield and Professor Gluckman comment:
Sister Hamill and Dr Stanhope appear to have misinterpreted the major theme of our paper. We addressed patient perception and satisfaction of growth hormone delivery systems, not growth hormone dose regimens. Publications to date have largely ignored patients' perception of growth hormone delivery. As the primary goal of growth hormone treatment is to promote greater psychosocial wellbeing, achieved in part by attempting to increase adult height, it is essential to consider patient acceptance of the method of treatment. In our study most children and their families preferred a pen to a syringe delivery system. As children self administered at an earlier age with the pen than with the syringe, we presume these are real differences perceived by the patients. If the prime motive of treatment is the improvement in psychosocial wellbeing, then use of the injector pen, despite a minor compromise in dose regimen, must be considered by the physician in the choice of treatment modality.

If there is a real advantage to the extreme accuracy of the regimens proposed by Hamill and Stanhope, hopefully pharmaceutical companies will respond by producing vials of varying growth hormone concentrations to allow more precise titration of dose using pens or other easy use administration devices.

Day case ligation of patent ductus arteriosus in preterm infants

SIR,—I read with interest about the brave new world of day case ligation of patent ductus arteriosus (PDA) in preterm infants[1] and was relieved to learn that infants were not discharged home on the day of surgery. The authors are to be commended on developing a safe and efficient service but are not justified in concluding in their abstract that 'if it is carried out early [ligation of PDA] will reduce the time before extubation and discharge from the intensive care unit'. They present no control data to support this conclusion. Indeed they refer in their discussion to a multicentre comparative study which showed no significant difference in mortality, duration of respiratory support, and number of days in hospital between infants receiving medical or surgical treatment.[2]

My own experience (also uncontrolled) over the last 10 years in a neonatal intensive care unit serving approximately 5500 births a year is that surgical ligation of PDA in preterm infants is very rarely necessary, only one infant having been operated on in the neonatal period. During this time we cared for 492 infants of birth weight ≤1500 g of which 173 had birth weight ≤1000 g. Our survival rates compare favourably with the other four large Trent region centres,[3] and long term ventilation (beyond 14 days) is now rarely needed.

Fluid restriction, early use of indomethacin, effective treatment of underlying lung disease including dexamethazone, and above all patience will allow the preterm infant's duct to close in all but exceptional cases. I am very worried at the apparent early resort to surgery which many appear to adopt.

It is not enough to show an operation is safe and readily available, it must also be shown to be necessary.

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Drs Satur and Dickinson comment:
As cardiologists and cardiac surgeons at a supraregional centre for paediatric cardiac surgery we see a highly selected group of preterm infants with a patent arterial duct, namely those referred by paediatricians specifically for ligation of the duct because the measures suggested by Dr Dodd had either failed or were considered inappropriate. Our conclusions at the end of the paper relate only to this group of patients. We have shown that if a paediatrician feels that active surgical management of the duct is necessary he or she should not delay because of the perceived hazards of transportation and operation. However we would agree entirely with the statement that the operation must be shown to be necessary. Because of the selected nature of our patients we cannot address the wider issues relating to the management of the patent arterial duct in the neonatal unit. We

are aware of differing rates of referral for ductal ligation from neonatal units within our own catchment area, but whether this is the result of different management or different case mix is uncertain. The statement in the abstract is, we agree, not supported by a controlled study, which we are not in a position to perform.

Absent or reversed end diastolic flow velocity in the umbilical artery and necrotising enterocolitis

SIR,—We read the paper of Malcolm *et al* with interest, and noted the close association between absent or reversed end diastolic flow (AREDF) velocities in the umbilical artery in high risk pregnancies and neonatal necrotising enterocolitis.[1] We wish to add some data that supports the hypothesis that it is AREDF, independent of growth retardation and prematurity, which predisposes to necrotising enterocolitis.

A prospective study of all patients attending a high risk fetal assessment clinic was performed over a two year period in this hospital. Umbilical artery flow velocity waveforms were studied using a Doppler Mark V Duplex scanner in pregnancies complicated by hypertension and/or intrauterine growth retardation. There were 20 cases where AREDF was identified in the umbilical artery of a morphologically normal fetus; of these, two were intrauterine deaths. The 18 liveborn fetuses were matched for gestational age and birth weight with 18 liveborn fetuses from the same cohort who had never had AREDF. The mean (SD) gestational ages were 32·2 (2·9) and 32·6 (1·9) weeks respectively for cases and controls and mean (SD) birth weights were 1323 (544) and 1489 (386) g. The mortality rate was 30% (6/20) for fetuses with AREDF; none of the controls died. Necrotising enterocolitis (defined as clinical features suggestive of necrotising enterocolitis confirmed by radiological evidence of intramural or portal air) occurred in four (22%) of the babies who had had AREDF compared with one (6%) of the control babies.

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1 Malcolm G, Ellwood D, Devonald K, Belby R, Henderson-Smart D. Absent or reversed end diastolic flow velocity in the umbilical artery and necrotising enterocolitis. *Arch Dis Child* 1991;**66**:805–7.

Body water measurements in growth disorders

SIR,—The ability of bioelectrical impedance to estimate body composition in the paediatric population is a subject of burgeoning interest. Two equations have now been published that relate height^2/impedance (H^2/I) to total body water by simple regression equations.[1 2] It is noteworthy that these two equations, based upon children with large variations in height, weight and age, are remarkably similar and this has led us to combine the raw data.

The new regression equation is therefore: total body water (litres)=0·13+0·58 H^2/I with a standard error of estimate of 1·3 litres.

This equation is based on 60 measurements of bioelectrical impedance and total body water using $H_2{}^{18}O$ isotopic dilution in children aged 5·2 to 17·9 years. It is hoped that this equation may be of use to those using impedance techniques in children.

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