Tests for growth hormone secretion

Str.—The reproducibility of pharmacological and physiological tests for growth hormone deficiency is rightly questioned in the annotation by Brook and Hindmarsh.1 The authors, however, do not consider the reproducibility of the measurement of height. We recently demonstrated the unavoidable imprecision of height measurement,2 and emphasise here its serious implications for the interpretation of short term growth data. We are particularly concerned about the estimation of velocity, where the errors from two height measurements rather than one are involved.

In their ‘plan for action’, Brook and Hindmarsh advise: Measure the child and . . . measure the child again after four months and calculate the annual velocity.3 To base a velocity on measurements four months apart greatly increases the error of measurement already associated with the estimation of velocity over 12 months. It has been shown that the SD for a single height measurement made by experienced observers lies in the region of 0·25 cm.4-6 (Any claim of a lower SD may well imply correlated measurement errors, as will happen, for example, if the calibration trials are not blind.) Given a typical SD of 0·25 cm, the 95% confidence interval for an annual velocity, calculated from the formula 2 (SD) CV 2, is the observed increment ± 0·71 cm/year. Where the measurements are only four months apart, instead of the standard 12, the confidence interval for an annual velocity triples in length. On this basis, the 95% confidence interval for a child between the ages of 5 and 6 years, estimated to be growing, for example, at the 50th centile for velocity, would lie between 4·2 and 8·4 cm/year, and more than span the whole centile range on the chart (A on the figure). A four month velocity cannot give any indication of current growth.

Furthermore, we have shown,7 and the authors have previously stated,7 that there is little correlation between successive height velocities. Velocity cannot therefore in practice be used to predict future growth. The appeal of errors discussed. The advantage is that all data points are used, including multiple measures on the same day. Growth velocity can then be calculated with an estimate of error.

A disproportionate emphasis is still placed on endocrine tests in establishing the need for growth hormone treatment. Our annotation sought to put this in perspective. As the Southampton group have demonstrated, growth measures are a lot more reliable than any of the current tests available for estimating growth hormone secretory status, placing auxology foremost in the assessment of growth and its disorders in children, even with the inaccuracies to which they have rightly drawn attention.

Gut blood flow velocities in the newborn

Str.—We read with interest the study by Coombs et al of the effects of parenteral indomethacin on splanchic blood flow.1 However we were surprised that no mention was made as to how the patency of the ductus arteriosus was established. In describing both the study and control groups the terms ‘sympathetic’ and ‘clinical’ lead to the assumption that echo Doppler cardiography was not performed. Surely in order to determine accurately the effect of a patent ductus arteriosus on splanchic blood flow, with or without parenteral indomethacin, it is essential to assess accurately the direction of flow and the pressure gradient across the ductus for both systole and diastole. The statements that: (1) indomethacin has effects on splanchic flow independent of its action on the ductus and (2) the slow administration of parenteral indomethacin shows no apparent loss of efficacy on ductal closure, cannot be concluded from this study and are potentially misleading due to the lack of accurate haemodynamic documentation.

95% confidence interval for an annual velocity based on two measurements of height, four months apart for: (A) a child estimated to be on the 50th centile for velocity; (B) a child estimated to be on the 3rd centile for velocity; and (C) a child with upper confidence limit for velocity on the 25th centile. The observed velocity lies below the first centile.

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8 Professor Brook and Dr Hindmarsh comment: The comments from the Southampton group are noted. As the article was directed at tests of growth hormone secretion our interests lay in the brief given rather than a discussion of errors of height measurement, which, as the authors point out, have been documented by groups in Switzerland and the United Kingdom. As they show, short term measures require different charts for decision making. In practice, however, growth rates less than the third centile nearly always indicate a clinical problem so we stand by our plan.

Dr Coombs comments: While echo Doppler cardiography may be the gold standard for diagnosing a patent ductus arteriosus, most UK neonatologists when deciding on the need for treatment rely, as we did, on the clinical findings of a characteristic murmur, baby pulseless, a wide pulse pressure, an increase in oxygen requirements, and evidence of heart failure. These clinical findings were present in all the babies comprising the study group and were not seen in the control group. Supporting, but not dispelling, the clinician’s decision to treat was the finding in the babies studied of the absence of retrograde diastolic flow in the superior mesenteric artery, an indication of left to right shunt.
The same criteria for ductal closure—disappearance of murmur, return of pulses to normal, and resolution of heart failure—were used in both studies and correlated with the return of diastolic flow. Although the numbers are small, there was no apparent difference in the efficacy between bolus and slowly infused indomethacin.

Our findings are that bolus indomethacin resulted in a pronounced fall in blood flow velocity in the superior mesenteric artery. We believe this fall in velocity represents a local vasoconstriction. This view is supported by animal and human data.\(^1,3\) and the observation that the magnitude of fall in velocity was different in the two vessels studied.

The important messages, however, are that with a patent ductus arteriosus the splanchic blood flow is compromised, and that slowly infused indomethacin avoids the profound fall in gut blood flow velocity that is seen with the first bolus dose of indomethacin.

Modern management of pyloric stenosis—must it always be surgical?

Sir,—The paper by Eriksen and Anders\(^1\) and the commentary\(^2\) interested us because the management of pyloric stenosis has often provoked controversy. In 1986 we also audited 62 cases presenting between 1979–85 to a mixed paediatric medical and surgical ward outwith the specialist paediatric surgical unit. Preoperative fluid and electrolyte replacement was managed by paediatricians and operations were performed by general surgeons. Prophylactic antibiotics were not given routinely.

Our audit emphasised the point made by all three contributors that the diagnosis of pyloric stenosis is not always straightforward. It also varies considerably in severity and so it was gratifying that Dr Jacoby's work\(^3\) was quoted by Mr Kiely.\(^4\) Although Jacoby operated on 104 babies with minimal morbidity and mortality there were a further 101 who tended to present later, have less severe vomiting, showed less weight loss and dehydration, and who responded rapidly and successfully to atropine methonitrate (Eumydrin).

In our series of 62 babies, seven were treated successfully with Eumydrin, had a very short hospital stay, and were treated pre-dominantly as outpatients for a mean of seven weeks (range 2–16). In 1987 Eumydrin was taken off the market, having been in use for 60 years. Paediatricians were thus denied the opportunity of avoiding surgery with its 24–50% complication rate. We would like to report that the product Pipitalin (Boehringer Mannheim), which contains the antispasmodic diphenylpiperazine bromide, has been used successfully in three babies with pyloric stenosis in the past 12 months. Nowadays few junior staff have any experience of judicious medical treatment for pyloric stenosis. Babies are, therefore, referred without a second thought for surgery, which fortunately carries a negligible mortality, although the complications described above should not be ignored.

Should medical treatment for pyloric stenosis be totally abandoned?

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Colloid babies with Gaucher’s disease—a further case

Sir,—Lui et al reported two neonatal siblings with ichthyosis and Gaucher’s disease who died in the first days of life.\(^1\) We wish to report another case.

Case report

The first child of a non-consanguineous white couple was born at appropriate weight for gestational age at 32 weeks’ gestation. There was no family history of birth defects, skin disorders, or haematological problems. At birth the baby had moderate ichthyosis with ectropion and some restriction of movement of the digits, presenting as a mild form of the ‘colloid baby’ phenotype. Hepatosplenomegaly was noted. The ichthyosis improved over the first 10 days, thrombocytopenia developed, and the baby's condition deteriorated with apnoea, suspected infection, and jaundice. Because of the report of Lui et al, leucocyte enzyme assays were performed and showed a gross deficiency in the \(\beta\) glucocerebrosidase activity measured with the natural \(\beta\) glucocerebroside substrate (53 pmol/min/mg protein, normal 60–3200) or the artificial 4mu substrate (19 pmol/min/mg protein, normal 60–220). The child died at the age of 3 weeks and postmortem liver histopathology confirmed a diagnosis of Gaucher’s disease.

This is the third reported case in the same city in Australia. The family in Lui et al came from the western suburbs of Sydney.\(^2\) The families were unrelated. We suspect that this diagnosis may be being overlooked in the differential diagnosis of ichthyosis in the neonatal period.

The reason for the association is by no means certain. Other associations with disorders of lipid metabolism and ichthyosis include X linked ichthyosis with steroid sulphatase deficiency, neutral lipid storage disease, Refsum's disease, and multiple sulphatase deficiency. Alternatively, it was suggested by Lui et al, the combination may represent manifestation of a contiguous gene disorder.\(^3\)

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BOOK REVIEWS


At last a readable book that paediatricians can recommend for general practitioners, health inspectors, and community medical officers undertaking child health surveillance.

The book is divided into two parts 'health promotion', which is further subdivided into primary, secondary, and tertiary prevention, and 'putting the programme into practice' which is split by developmental stages up to school entry. The latter has a very basic 'what to do' and 'how to do it' approach to commonly encountered clinical problems that will suit those new to surveillance.

The child psychiatry input to the assessment and management of common behaviour problems is particularly valuable and will add greatly to the practical value of the book. The flow diagrams and diary suggestions should lead to successful resolution of many of these types of disorder.

No book of this size could claim to be comprehensive, and personally I would have liked a larger section on breast feeding and management of breast feeding related problems, the effects on children of separation and divorce,