An assessment of growth hormone provocation tests

features are poor indicators of the diagnosis or whether there is an isolated or multiple pituitary deficiency. In the neonatal period and after cranial irradiation there are clearer indications for testing.

The authors consider that growth hormone measurements remain a valid investigation in order to provide biochemical support for subsequent growth hormone treatment. Despite the statistical constraints of the tests the likelihood that a slowly growing child is growth hormone insufficient is increased twofold in the presence of a positive test but only decreased by half in the presence of a negative one. Improving the probability of the presence of a growth hormone secretary disorder is particularly important if general practitioners are to be asked to prescribe and, therefore, to take some shared responsibility for the prescription. Also, detailed evaluation would seem to be a prerequisite for outcome audit and research purposes. Advances in cellular and molecular biology will gradually clarify the diagnosis of idiopathic isolated growth hormone insufficiency but these techniques will only be as good as the defined phenotype.

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Commentary

It is now more than 30 years since the induction of hypoglycaemia was described as a way of manipulating growth hormone secretion.1 The ITT, which can also provide an assessment of ACTH reserve, has been an established method to measure growth hormone secretion primarily in short children and stress related cortisol secretion primarily in adults with pituitary disorders. The Health Services Human Growth Hormone Committee was a government quango which was remarkably effective in maintaining a satisfactory standard of investigation for short children who might benefit from growth hormone treatment.2 When the government in its wisdom disbanded the quango, an internationally recognised UK database of adequately investigated children receiving growth hormone treatment soon disappeared. To its credit, the Kabi Pharmacia
International Growth Study has been the only attempt to partially restore this valuable resource. In the meantime, the paediatrician has been faced with a plethora of growth hormone tests from which to choose one which is efficient and safe. Safety is of paramount importance whatever the nature of the clinical investigation is; it is therefore not surprising that the ITT is currently less favoured as a test of growth hormone secretion in children in view of a recent report which highlights the dangers of the procedure when the test is performed incorrectly.

Hindmarsh and Swift have produced a further review of growth hormone tests for paediatricians to consider. A novel feature of this one is the attempt to use standard validation criteria of a diagnostic test (that is sensitivity, specificity, and coefficients of variation) in comparing the growth hormone measurement with growth rate. An ambitious idea as growth is an amalgam of genetic, nutritional, hormonal, metabolic, and psychosocial influences. Nevertheless, their review does offer a pragmatic approach to the interpretation of growth hormone tests that can be used by paediatricians, be they working in general or specialised units. After all, short children are commonplace and enter the practice arena of all paediatricians. The ideal goal is to identify a single bioassay or marker of growth hormone production and action that is relevant to growth. Improved knowledge of the neuroendocrine control of growth hormone secretion and its mode of action has spawned a number of promising markers of growth hormone secretion such as IGF-1 and its binding proteins.

However, none of these measurements will substitute for the additional information which can be obtained about pituitary function when employing the ITT. Adult endocrinologists have shown the way by reporting audits of their experience with the ITT. While accepting that the clinical indications for using this test are usually different in adults and children, paediatricians should now also audit their practice with the ITT before finally deciding on their idealised ‘gold standard’ of growth hormone secretion. The stimulus for my producing a series of endocrine menus protocols and case histories arose out of concern for how many children were being investigated inappropriately and required re-investigation. Whichever growth hormone test is chosen and wherever it is performed, we owe it to our patients to ensure meticulous attention to protocol details and supervision by staff who understand the rationale for the investigation.

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