Short reports

Exercise test for growth hormone deficiency

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SUMMARY An exercise test measuring energy expenditure was performed on a bicycle ergometer by 98 patients in the outpatient clinic. Results concordant with the final diagnosis were obtained in 89% of the 75 children referred because of short stature and in 65% of the 23 children with associated chronic disorders.

The climate of opinion is moving towards greater use of physiological tests in suspected growth hormone deficiency, and exercise has been recommended by the Health Services Human Growth Hormone Committee¹ for the early investigation of this disorder in patients in district general hospitals. A plasma growth hormone concentration of 15 mU/l or more is considered to exclude deficiency.

Exercise, as a stimulus to growth hormone secretion in the investigation of short stature, was recommended more than 10 years ago.^{2,3} Exercise tests, however, have never attained great popularity because of a reputation for giving false low results.^{4,5} A physiological study of adults showing that stimulation of growth hormone was directly proportional to the energy expenditure and that hard exercise compared favourably with biochemical tests, influenced us to set exercise targets for children which ensured maximum effort.⁶

Patients and method

Since 1978 we have carried out exercise tests in the outpatient clinic on 98 children—about one in four of those referred because of short stature. In most children height velocities less than the 25th centile had been recorded over a 12 month period before the test, but a number of children, especially teenage boys, who were very anxious about their height, were checked earlier so that they could be reassured.

A Puch Tunturi bicycle ergometer was used. This measured the duration of exercise, resistance against pedalling (in kiloponds), the speed of the

revolutions, and the distance travelled (in kilometres). The children were encouraged to exercise as hard as possible, regarding the test as a competitive game. After 10 minutes they were hot, flushed, and sweating but not exhausted. Growth hormone was estimated by radioimmunoassay using the standard First International Reference Preparation of human growth hormone. The following protocol was used for the exercise test:

- (1) Adjust the saddle height, record the reading on the distance indicator, note the time, and set the alarm bell to ring in 10 minutes;
- (2) Ask the child to start pedalling and adjust the resistance to a suitable level, usually 2 kiloponds at the age of 10 to 12 years (1.5 for younger children or up to 4 for adolescents);
- (3) Encourage the child to maintain a speed of 25 km/hour throughout the test;
- (4) When the alarm bell rings note the distance travelled (usually about 4 km);
- (5) Exactly 25 minutes from the *start* of the exercise, take 3 ml of blood for growth hormone determination;
- (6) Calculate the work performed in kilopond metres (resistance $\times$ distance travelled in metres).

Results

Patients later diagnosed as growth hormone deficient because of a height velocity during one year of less than the 25th centile and a growth hormone response to adequate insulin hypoglycaemia of less than 15.0 mU/l had shown uniformly low responses to the exercise test. They were supplied with growth hormone by the Health Services Human Growth Hormone Committee and all showed the increased height velocity required for treatment to be continued after the first year. (See Table.) The small group with a height less than the third centile and a bone age delay less than two years responded very well, except for one boy of 6 years in whom a repeat test a year later was normal. The small-delay group with a height less than the third centile and a bone age delay

Table Growth hormone response to exercise

Group	Total	Distribution of growth hormone responses (mU/l)				
		Abnormal			Normal	
		0-5	5-10	10-15	15-20	>20
Growth hormone deficient	9	6	3	0	0	0
Small	27	0	0	1	5	21
Small-delay	39	0	1	6	6	26
Miscellaneous	23	1	4	3	5	10

greater than two years responded less well. Several had delayed puberty and repeat tests with sex steroid priming were normal. Others gave a satisfactory response to a biochemical test. Taking these three groups together, 67 of 75 gave results concordant with the final diagnosis (89%). It was thought that growth hormone deficiency might contribute to the short stature of a miscellaneous group of 15 patients with chronic disorders, for example, hydrocephalus, coeliac disease, anorexia nervosa, asthma, and Turner's syndrome. Eleven responded well. In addition, four of eight children who had completed a course of treatment for acute lymphatic leukaemia, which included intracranial radiation, responded normally. Overall, growth hormone deficiency was excluded in 15 of 23 children (65%).

The Figure provides a useful guide to the exercise targets required to produce an adequate growth hormone response. The work performed increases

Figure Work performed—kilopond metres in 10 minutes.

with age throughout childhood, and dramatically so in teenage boys. Most of those who failed to achieve a normal growth hormone response but who were later proved not to be growth hormone deficient reached lower work targets.

Discussion

Our early experience with exercise tests was disappointing. Results improved considerably after we adopted the precise instructions in the protocol. No previous report has given details of how children may be encouraged to achieve the maximal energy expenditure essential. Calculation of the work done may show a relatively poor performance and, if so, a repeat test is often successful.

Results concordant with the final diagnosis were obtained in 89% of first exercise tests carried out to distinguish children with constitutional short stature in the small and small-delay groups from those with growth hormone deficiency. This is the same order of success as claimed for biochemical tests. In addition, the exercise test was of value in excluding growth hormone deficiency as a contributing cause of short stature in 65% of a miscellaneous group of children with chronic disorders.

The exercise test is physiological, safe, simple to perform, cheap, and relatively pleasant for the child. In our experience its use has greatly reduced the number of children requiring other investigative procedures, for example the sleep, clonidine, L-dopa, arginine, glucagon, and insulin hypoglycaemia tests, which entail multiple blood sampling and often admission to hospital. The protocol should facilitate its successful use by doctors at present unfamiliar with the procedure.

We thank Miss Browning and staff, Department of Biochemical Medicine, Ninewells Hospital for the growth hormone estimations.

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Received 13 September 1984