

The Effect of Nor-androstenolone Phenylpropionate (Durabolin®) on Children with Retarded Growth

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Much forethought and circumspection are required in the treatment of children with retarded growth because the drugs currently applied not infrequently exert side effects that upset the endocrine balance. The first vital question to arise is that of the lower limits under which treatment appears justified. No doubt, in dwarfism provided that factors other than genetic are responsible for it, a causal therapy should first be attempted. Dwarfism is a rare syndrome; NOBEL et al. [1] take it as existent in the child when the lag behind normal growth exceeds 30 per cent; FANCONI and PRADER [2] draw the line at 40 per cent; but growth lags of this extent are seldom encountered. Of the diseases of the endocrine glands, aplasia of the thyroid gland, severe hypothyroidism, and hypofunction of the pituitary body can cause dwarfism, but lags behind normal height due to hypopituitarism are usually less than 40 per cent wherefore such children cannot be regarded as cases of true dwarfism.

In our material mostly children with growth lags between 10 and 25 per cent and no arrested mental development are requiring treatment.

For example, a girl patient, 8 years of age and only 105 cm tall instead of 128 cm, who impressed one as not more than 4 years old, would have been seriously hampered in life by this less than normal height, and so was undoubtedly entitled to treatment.

Some types of retarded growth hardly come into consideration for treatment. Among these we would place primordial, dwarfs and growth disturbances due to anomalies of the skeletal system, such as chondrodys-trophic dwarfism, osteogenesis imperfecta, etc.

Accessible to treatment are, or should be, growth lags due to nutritional deficiencies or insufficient functioning of the endocrine glands. Cases due to the first-mentioned cause naturally require causal treatment and an appropriate diet. In the case of insufficient functioning of the endocrine glands causal treatment consists in the application of an adequate substitutive therapy. This will generally answer the case in hypothyroidism, but where a dysfunction of the pituitary is the cause of retarded growth the situation is somewhat

complicated because the growth hormone preparations now available have failed in ensuring favourable results. In some of these cases, provided at least one symptom of hypothyroidism prevails, such as a retardation in the development of ossification centres, success can be achieved by thyroid preparations, in others by the administration of thyrotrophic hormone, yet in others by gonadotrophin. In view of the hypogenitalism present in many of these patients, all these treatments have passed as partly causal cures. However, more often than not they fail to give reasonable satisfaction. This fact has led to the widespread employment of testosterone preparations which owing primarily to their intensive anabolic effect are capable of promoting development both in weight and height. On the other hand, if these preparations are considered from the point of view of their hormonal action, their use cannot be regarded as causal therapy. In addition, they adversely affect the development of the gonads (which are usually underdeveloped in such patients) for the hormone introduced depresses gonadal function. Besides, testosterone preparations exert untoward side-effects; their enhancing the development of secondary sexual characteristics sets limits to their use; in girls, their application commands particular care because of their tendency to produce virilism.

In the present situation much is expected from nor-androstenolone phenylpropionate as a growth promoter. This compound was reported

to exert an enhancing effect on anabolism four times that of testosterone phenylpropionate, without interfering with sexual development. In children with their growth retarded in consequence of some chronic disease it produced gains in weight [3]. It favourably influenced development of premature and dystrophic infants [4]. It was observed more intensely to enhance weight gain than growth, yet to promote growth even in hypophyseal dwarfism [5].

The present paper is a report of our results achieved with nor-androstenolone phenylpropionate.

PATIENT MATERIAL

Twenty-nine children admitted to this Department in the last 18 months because of retarded growth were treated. None of them showed developmental anomalies, symptoms of hypothyroidism, or some intercurrent disease as the cause of retarded growth.

The weight and height of our patients recorded before and after treatment were compared with the data for normal children published by the Harvard School of Public Health [6], which according to FANCONI and PRADER [2] correspond to the findings for normal Swiss children, and according to GARAMVÖLGYI [7] approach those for the children in Hungary.

Of the 29 children 18 were treated for periods of 6 to 12 months and 11 for less than 6 months. Of the patients treated for more than 6 months, in 6

TABLE 1

Effect of Nor-andröstenolone Phenylpropionate on Height and Weight Development
Date recorded before and after treatment in comparison with the Harvard data for normal children (6)

Case No.	Age in years, sex	Lag BEFORE TREATMENT behind				Increment AFTER			TREATMENT			Duration of treatment, months	Courses of treatment
		normal length		normal weight		length			weight				
		cm	%	kg	%	cm	excess over normal		kg	excess over normal			
							cm	%		kg	%		
1	7 ♂	16.9	13.6	6.5	27	8.0	+2.1	14	6.5	+4.0	160	12	3
2	7 ♂	9.1	7.3	3.4	14	4.0	+1.0	33	1.7	+0.4	35	6	2
3	10 ♂	18.3	13.0	12.6	39	3.5	+1.5	75	2.6	+1.4	50	7	3
4	7 ♂	24.6	19.8	8.54	35	1.5	—1.5	—	1.0	—0.4	—	6	2
5	10 ♀	30.6	23.0	15.3	49	5.0	+2.3	80	2.5	+1.8	200	7	3
6	8 ♀	23.0	17.8	10.35	39	6.0	+1.1	22	4.0	+2.2	120	12	3
7	3 ♂	13.2	13.5	4.91	35	7.0	+3.4	94	2.5	+2.0	400	8	2
8	7 ♂	20.6	17.0	8.0	33	9.5	+4.5	90	6.0	+3.0	100	10	3
9	9 ♂	15.5	11.5	8.9	30	9.0	+4.5	90	4.5	+2.3	100	14	3
10	12 ♂	24.6	16.5	11.2	29.7	4.0	—0.9	—	2.5	+0.5	25	11	2
11	7 ♂	15.1	12.0	4.5	19	2.0	—2.0	—	2.2	+0.9	70	8	3
12	4 ♂	4.4	4.0	3.5	21	7.0	+3.9	125	2.5	+1.5	150	6	2
13	10 ♀	26.6	19.0	10.8	33	7.0	+2.0	40	5.1	+3.0	140	10	3
14	5 ♂	10.3	9.2	3.8	25	8.0	+1.8	29	2.9	+0.5	17	12	3
15	6 ♂	4.5	3.8	3.71	17	8.0	+2.5	45	4.8	+3.0	160	12	3
16	8 ♀	19.5	15.0	10.35	39	3.5	+1.0	40	4.0	+3.5	650	6	2
17	15 ♂	27.8	16.0	24.48	45	5.0	+2.6	105	4.5	+2.3	100	8	3
18	5 ♀	12.7	11.5	2.87	15	4.0	+0.9	22	2.0	+0.5	33	6	2

the retardation of growth varied between 15 and 23 per cent, in 8 between 10 and 15 per cent, and was less than 10 per cent in 4 patients. The latter obviously were children small for their age, and only the former, with growth lags of 30 cm and 15 cm, respectively, were considered "pathologically underdeveloped". With the exception of one child all the others treated for less than 6 months belonged in the group of "pathologically underdeveloped" patients. The retardation to weight development was mostly more signif-

icant than that in growth. In most children of the pathologically underdeveloped group ossification was retarded, but no marked disproportionality was noted; clinically, the underdevelopment in this group was most probably of hypophyseal origin.

A 10 to 12.5 mg dose of nor-androstenolone phenylpropionate preparation Durabolin® (Organon, Oss, Netherlands) was administered intravenously every fifth day for a period of six weeks. Following a rest period of from six weeks to three month the treatment was repeated.

TABLE 2

Comparison of Percentile Retardation in Height and Weight before and after Nor-androstenolone Phenylpropionate Treatment in Relation to Harvard Data for Normal Children (6)

Case No.	Percentile retardation			
	height		weight	
	before treatment	after treatment	before treatment	after treatment
1	13,6	11,5	27	11,4
2	7,3	6,3	14	12,7
3	13,0	11,8	39	31,8
4	19,8	20,0	35	35
5	23,0	20,3	49	44
6	17,8	16,5	39	31,4
7	13,5	9,8	35	18,6
8	17,0	10,9	33	16,6
9	11,5	8,0	30,6	22
10	16,44	16,5	29,7	30
11	12,0	13	19	17
12	4,0	0,6	21	12,9
13	19,0	15,5	33	24
14	9,2	5,5	25	21
15	3,8	2,5	17	6
16	15,0	13,0	39	28
17	16,0	14,6	45	39
18	11,5	10	15	13

RESULTS

On the evidence of the data presented in Table 1, in 14 of the group of 18 patients treated for periods of 6 to 12 months, i. e. given two or more six-week treatments with rest periods between them, the rates of growth significantly exceeded those considered normal [6] for the corresponding age periods; these included five of those six subjects who in growth had lagged more than 15 per cent behind normal before Durabolin® therapy was instituted, leaving only one with less than the physiological growth increment. In two of this group growth occurred at the normal rate, and in two it was less.

A remarkable case was No. 8 in Table 1. Prior to treatment, this child showed 17 per cent retardation in

growth but during a 10 month period of treatment it gained 9.5 cm in height (which is 4.5 cm in excess of the normal) and added 6 kg to its weight.

Gains in weight were on the whole more substantial in this group than were gains in height, but the two ran parallel courses; this is to mean that lesser gains in weight went hand in hand with less significant gains in height. It can be seen from Table 2 that in both weight and height the overwhelming majority of our patients lagged much less behind the normal after treatment than before it; a fact which undoubtedly points to the favourable action of Durabolin®. (With Student's single-pattern t test: $p < 0.1\%$.) Of course, in these cases statistical evaluation cannot be accepted without certain considerations.

TABLE 3

Effect of Nor-androstenolone Phenylpropionate Treatment for Less than 6 Months on Growth and Weight

Case No.	Age in years, sex	Retardation before treatment				Gain after treatment		Duration of treatment, months
		length		weight		length cm	weight kg	
		cm	cm%	kg	kg %			
1	13 ♂	17,5	11,3	17,0	40,0	1,5	1,5	2
2	7 ♀	16,0	13,0	8,0	34,7	3,0	3,5	3
3	14 ♀	43,0	27,0	22,4	50,0	2,5	2,5	5
4	12 ♂	23,4	15,7	15,5	40,8	3,0	3,3	4
5	8 ♀	13,0	10,1	11,3	43,0	1,0	2,5	1 ½
6	6 ♀	5,0	4,0	6,0	28,0	1,0	2,5	2
7	12 ♀	20,0	13,0	13,0	33,0	1,0	2,0	3
8	7 ♀	24,0	20,0	9,0	39,0	3,5	2,8	2
9	7 ♂	20,5	16,0	8,0	33,0	3,0	1,1	4
10	14 ♀	25,5	16,0	11,0	22,0	1,5	2,5	2
11	15 ♂	14,0	8,6	10,0	20,0	3,0	3,4	2

We have no means to know how the children would have developed had they received no Durabolin® treatment. As, however, in our patient material growth had been retarded for several years past, it seems obvious that despite expectations to the contrary there was more than usually accelerated growth in height under the action of Durabolin®.

The results listed in Table 3 show that the drug exerted a similarly favourable effect in all our patients treated for periods of not more than six months. They also furnish evidence that the more significant the growth increments, the more substantial were the accompanying gains in weight.

Twenty-one patients were examined for the effect of Durabolin® as early as two months after treatment had begun. In 16 of them the gain in height was less than 2 cm, but only one child gained in weight less than 1 kg. Gain in weight was found to be considerable throughout; on the evi-

dence of the data in Table 3, only in two of 11 patient treated for periods from 6 weeks to 5 months was the weight increment in kg less than the height increment in cm whereas it is common knowledge that in normally developing children the number of kilograms gained is generally half the number of centimeters grown.

No side-effects were noted in the children treated for less than 6 months, but some were observed in 8 of the patients subjected to two or more courses of treatment over periods longer than 6 months. In 6 boys (3, 5, 6, 7, 7 and 15 years old) there was enlargement of the penis and, according to their parents, erections occurred from time to time. In 2 girls, aged 8 and 15 years, there was slight development of pubic hair.

These side-effects may set limits to the use of the drug: it will sometimes be necessary to reduce the dose or lengthen the interval between cures.

SUMMARY

In children with retarded growth nor-androstenolone phenylpropionate administered in doses of 10 to 12.5 mg intramuscularly every five days for six weeks, has been found significantly to promote development

in both height and weight. Its primary and more vigorous action was to increase body weight. Two courses of treatment were often needed for the favourable effect of the drug to manifest itself.

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