Growth Curves for Height for Diastrophic Dysplasia, Spondyloepiphyseal Dysplasia Congenita, and Pseudoachondroplasia

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• **Analysis of retrospective growth data from 72 patients with diastrophic dysplasia, 62 patients with spondyloepiphyseal dysplasia congenita and 61 patients with pseudoachondroplasia permitted the establishment of preliminary reference growth standards for height for each disorder. In addition, a comparison of mean height curves for these three disorders and achondroplasia revealed dissimilarities in growth patterns.**

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Growth curves, which allow a short-statured child to be compared with his or her similarly affected peers rather than with the normal-statured population, have proven useful in the management of achondroplasia.[1] Similar curves would be helpful in dealing with other forms of short stature; however, they are not currently available. To fill this need, we have combined retrospective growth data on patients with a number of less common skeletal dysplasias from five institutions. The data were sufficient to construct preliminary curves of height vs age for three of the disorders: diastrophic dysplasia, spondyloepiphyseal dysplasia congenita, and pseudoachondroplasia. Comparison of the curves revealed slight differences in the growth patterns of the disorders.

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METHODS

Measurements of total height were obtained from records at genetics clinics at the University of Kansas School of Medicine, Kansas City; University of Washington School of Medicine, Seattle; University of Texas School of Medicine, Houston; Johns Hopkins University School of Medicine, Baltimore; and Harbor-UCLA Medical Center, Torrance, Calif. Only patients meeting strict clinical and roentgenographic criteria for the diagnosis of each of the disorders were included.[2,3] If a patient had received a potential growth-promoting drug, such as halodrin (fluoxymesterone), only those measurements taken before drug administration were used. Most of the measurements were made during routine clinic visits. However, these clinics specialize in the evaluation of short stature and attempt to standardize their measurement methods.

The data were obtained from 72 patients (38 boys and 34 girls) with diastrophic dysplasia, 62 patients (34 boys and 28 girls) with spondyloepiphyseal dysplasia, and 61 patients (28 boys and 33 girls) with pseudoachondroplasia. Longitudinal data were available for some patients. In most cases, the data comprised either a single measurement or measurements separated by many years that were considered as isolated values.

Graphic methods were used to construct the curves.[4,5] Briefly, for each disorder all measurements were plotted in a scattergram so that the general shape of the curve could be determined. This method was used to adjust individual points to the nearest age at which a mean and an SD were calculated. These reference ages were birth, 6 months, 1 year, 2 years, and each even year through the age of 18 years, when skeletal growth was considered to be complete. At some ages, especially during the middleteen years, only two or three measurements had been made for boys and girls together, and there were nine instances in which either no data or only a single measurement was available for one sex or the other. Therefore, male and female measurements were combined. Rough curves were determined from the calculated values. They were then

Mean Heights in Diastrophic Dysplasia, Spondyloepiphyseal Dysplasia, and Pseudoachondroplasia

	Diastrophic Dysplasia (n = 72)*			Spondyloepiphyseal Dysplasia (n = 62)*			Pseudoachondroplasia (n = 61)*		
	No. of OBS,	Height, cm		No. of OBS,	Height, cm		No. of OBS,	Height, cm	
Age, yr	M + F†	Mean	SD	M + F	Mean	SD	M + F	Mean	SD
Birth	12 + 12	41.67	4.69	9 + 5	42.14	2.66	8 + 10	49.39	1.97
6 mo	3 + 0	56.33	1.15	3 + 2	48.00	3.03	2 + 4	63.17	2.86
1	3 + 2	63.40	5.94	2 + 1	58.67	4.04	0 + 6	71.17	1.47
2	3 + 3	70.00	5.51	8 + 5	68.23	4.94	2 + 7	80.22	3.07
4	6 + 7	82.69	6.25	12 + 5	80.00	8.24	4 + 7	88.73	3.07
6	8 + 7	90.87	7.61	8 + 5	88.38	7.01	5 + 6	94.55	3.86
8	5 + 10	100.27	8.50	6 + 7	94.23	11.53	4 + 4	98.13	5.69
10	4 + 5	103.89	9.99	7 + 7	99.43	11.10	2 + 8	106.80	6.41
12	7 + 3	102.90	10.95	7 + 0	106.57	14.73	2 + 5	111.14	9.96
14	7 + 1	104.88	9.93	6 + 3	114.56	19.79	1 + 2	124.00	2.00
16	2 + 1	112.67	13.43	3 + 0	120.33	15.82	0 + 2	120.50	14.85
18	12 + 9	118.33	12.03	9 + 9	115.50	14.88	11 + 19	118.83	12.22

*Figure in parentheses is number of patients from whom measurements were made.
†Number of observations (OBS) that contributed to means and SDs broken down by sex.

smoothed to compensate for differences in the size of the SDs. The means, plus or minus 1 SD, were plotted on the final curves. For comparison, a standard normal curve depicting the 50th, 95th, and 5th percentiles was prepared by averaging normal male and female height derived from the National Center for Health Statistics (NCHS) Growth Curves.[6] To determine if differences in height reduction existed between boys and girls for each disorder, all measurements at each reference age were converted to Z scores (patient height minus NCHS mean height, divided by NCHS SD). These values were combined and averaged for each sex for comparison.

RESULTS

The mean heights, SDs, and number of observations (broken down by sex) at each reference age are shown for each disorder in the Table. The mean Z scores for boys and girls, respectively, were −5.58 and −5.52 for diastrophic dysplasia, −6.28 and −5.78 for spondyloepiphyseal dysplasia congenita, and −4.46 and −4.21 for pseudoachondroplasia. In no case was the difference statistically significant.

The height curve for diastrophic dysplasia is shown in Fig 1. The range of birth length overlapped slightly with the lower limit of normal, but with time, the length (height) progressively fell below the normal range. Figure 2 illustrates the height curve for spondyloepiphyseal dysplasia congenita. Although there was no overlap with normal at birth, the shape of the curve for spondyloepiphyseal dysplasia congenita resembled that for diastrophic dysplasia. The height curve for pseudoachondroplasia is displayed in Fig 3. The length at birth and during infancy was within the normal range. Although the mean height began to drop away from normal immediately after birth, it was not until after the age of 2 years that a dramatic drop-off was observed.

Curves depicting the mean heights for all three disorders, as well as for achondroplasia (calculated from averaged male and female values previously reported[1]), are illustrated in Fig 4. The curves for diastrophic dysplasia and spondyloepiphyseal dysplasia congenita were quite similar, except that the mean height for the former was slightly greater at all ages. The average length (height) for pseudoachondroplasia was greater than that of the other conditions during infancy. After 2 years of age, however, the growth rate of children with pseudoachondroplasia decelerated more rapidly than that of the other conditions; by the age of 18 years the average heights were similar in pseudoachondroplasia, diastrophic dysplasia, and spondyloepiphyseal dysplasia congenita. In contrast, children with achondroplasia grew at a greater rate after infancy and attained a slightly taller adult height.

COMMENT

Growth curves for height have been constructed for diastrophic dysplasia, spondyloepiphyseal dysplasia congenita, and pseudoachondroplasia. They are preliminary curves based on a limited number of measurements recorded from a relatively small number of patients. In contrast to a similar study in which reference standards for height were determined for achondroplasia,[1] the sample sizes in this investigation were much smaller: achondroplasia, 403 patients; diastrophic dysplasia, 72 patients; spondyloepiphyseal dysplasia congenita, 62 patients; and pseudoachondroplasia, 61 patients. Although construction of separate curves for each sex would have been ideal, too few measurements were available, especially during the adolescent period, to permit such a procedure. Ironically, the need for separate curves is greatest during this period. There was no evidence that sex influenced the degree of stature shortening in any of the disorders.

Only 1 SD was plotted on the curves, since relatively large SDs compared with normal were obtained. A number of factors in addition to small sample sizes probably contributed to the large values. Measurement errors likely occurred despite attempts to minimize them. Deformities that accompany the individual disor-

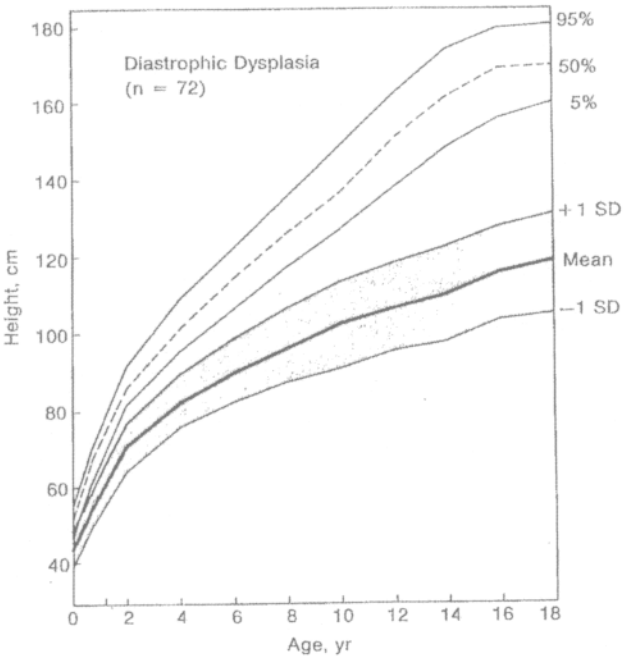

Fig 1.—Growth curve for height for patients with diastrophic dysplasia (shaded area).

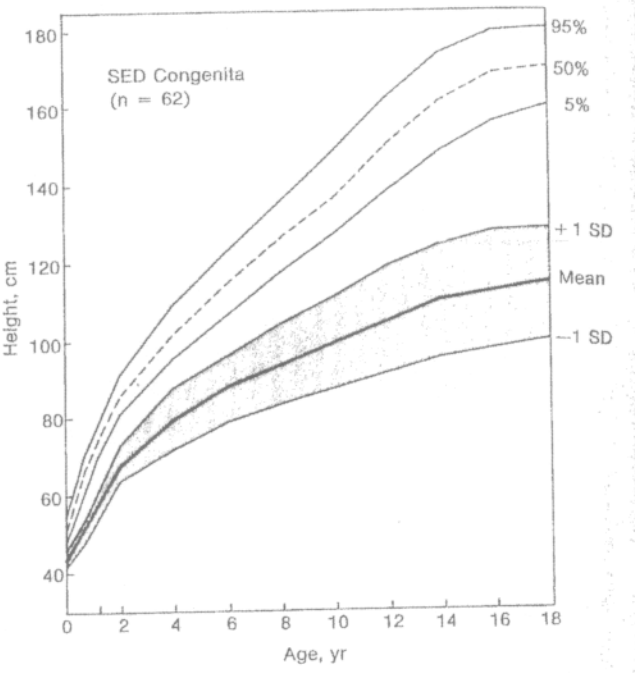

Fig 2.—Growth curve for height for patients with spondyloepiphyseal dysplasia (SED) congenita (shaded area).

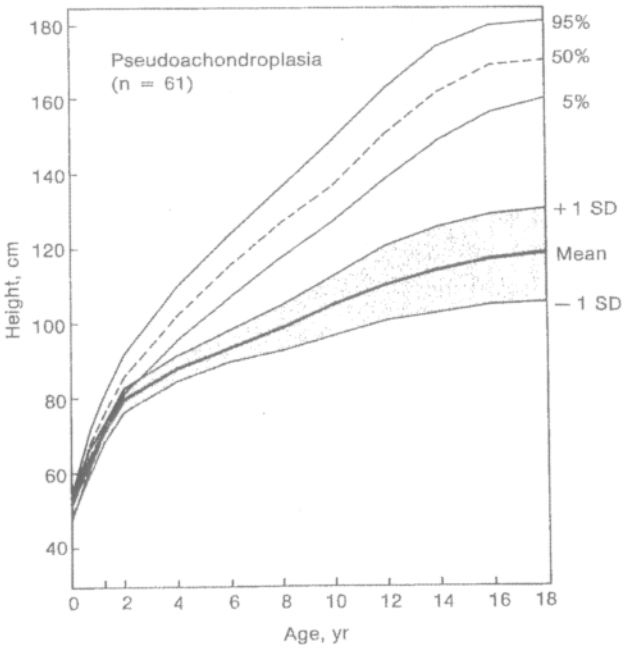

Fig 3.—Growth curve for height for patients with pseudoachondroplasia (shaded area).

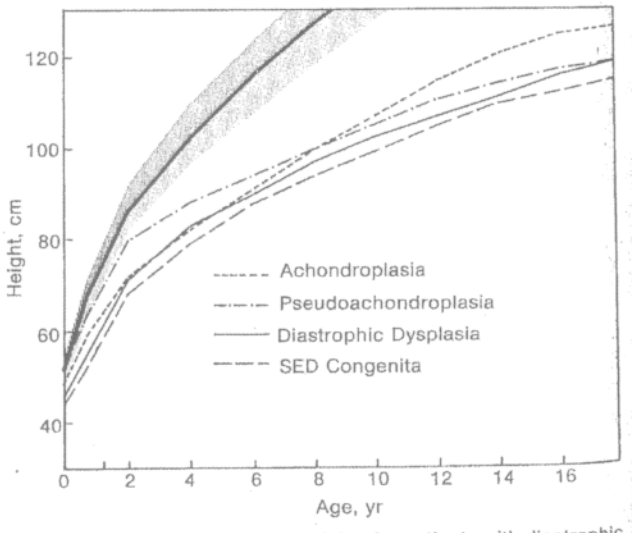

Fig 4.—Curves depicting mean heights for patients with diastrophic dysplasia, spondyloepiphyseal dysplasia (SED) congenita, pseudoachondroplasia, and achondroplasia. Shaded area indicates normal growth curve.

ders, such as scoliosis or contractures, and surgical treatments for deformities, eg, spinal fusion, must have played a role as well. In addition, genetic heterogeneity, which may exist within certain of the conditions, such as pseudoachondroplasia and spondyloepiphyseal dysplasia congenita, could have contributed.[2,7] Heterogeneity was not taken into account because it is not well defined or clinically recognizable in any of the disorders.

Despite these reservations, we think that the curves are useful. They provide reference growth standards with which the growth of a child with one of the disorders can be compared.

The knowledge that the child is growing within the "normal range" for his or her condition should comfort the anxious patient and parents, as well as physicians caring for the child. Conversely, if a child's height differs substantially from that expected from the curves, additional factors that interfere with growth should be sought or the patient may have another disorder.

The curves permit the growth patterns of the different disorders to be compared. For example, the curves depicting the mean heights at different ages for diastrophic dysplasia and spondyloepiphyseal dysplasia congenita are quite similar. The shapes of the curves for pseudoachondroplasia and achondroplasia differ slightly, however. In the former, the growth rate during infancy is almost normal but drops off dramatically after the age of 2 years. In contrast, even though the birth length and growth rate during infancy are less, the average child with achondroplasia reaches a greater adult height because the growth rate is greater between the ages of 2 and 18 years than in pseudoachondroplasia. These dissimilar growth patterns presumably reflect the different ways in which the two basic defects influence the normal growth process. It should be pointed out, however, that when variability is considered, there is actually little difference in height among the four disorders except at birth and during infancy, when infants with pseudoachondroplasia fall within the normal range.

Finally, we hope that the publication of these curves will stimulate the collection of prospective longitudinal growth data in patients with these three disorders and other skeletal dysplasias. Only through the careful measurement and recording of length (height) and other growth measurements can definitive reference standards for both boys and girls be established for these disorders.

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References

1. Horton WA, Rotter JI, Rimoin DL, et al: Standard growth curves in achondroplasia. *J Pediatr* 1978;93:435-438.
2. Rimoin DL: The chondrodystrophies. *Adv Hum Genet* 1975;5:1-118.
3. Spranger JW, Langer LO, Wiedemann HR: *Bone Dysplasias: An Atlas of Constitutional Disorders of Skeletal Development.* Philadelphia, WB Saunders Co, 1974.
4. Tanner JM, Whitehouse RH, Takaishi M: Standards from birth to maturity for height, weight, height velocity, and weight velocity: British children, 1965: I. *Arch Dis Child* 1966;41:454-471.
5. Tanner JM, Whitehouse RH, Takaishi M: Standards from birth to maturity for height, weight, height velocity, and weight velocity: British children, 1965: II. *Arch Dis Child* 1966;41:613-635.
6. *National Center for Health Statistics Growth Charts.* National Center for Health Statistics, 1976, vol 25, suppl HRA 76-1120.
7. Hall JG, Dorst JP: Four types of pseudoachondroplasic spondyloepiphysial dysplasia (SED). *Birth Defects* 1969;5:242-259.

CORRECTION

Word Omitted.—In the review by William W. Cleveland, MD, of *Pediatric Endocrinology* by S. Douglas Frasier, MD, in the December JOURNAL (1981;135:1156), the word "not" had been omitted; the last sentence should have read as follows: "All in all, I consider this book a valuable addition to existing textbooks in pediatric endocrinology; it is especially useful for physicians and students who are not deeply involved in the discipline."