ORIGINAL ARTICLE

Growth charts for Down's syndrome from birth to 18 years of age

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Background: Growth in children with Down's syndrome (DS) differs markedly from that of normal children. The use of DS specific growth charts is important for diagnosis of associated diseases, such as coeliac disease and hypothyroidism, which may further impair growth.
Aims: To present Swedish DS specific growth charts.
Methods: The growth charts are based on a combination of longitudinal and cross sectional data from 4832 examinations of 354 individuals with DS (203 males, 151 females), born in 1970–97.
Results: Mean birth length was 48 cm in both sexes. Final height, 161.5 cm for males and 147.5 cm for females, was reached at relatively young ages, 16 and 15 years, respectively. Mean birth weight was 3.0 kg for boys and 2.9 kg for girls. A body mass index (BMI) >25 kg/m^2 at 18 years of age was observed in 31% of the males and 36% of the females. Head growth was impaired, resulting in a SDS for head circumference of –0.5 (Swedish standard) at birth decreasing to –2.0 at 4 years of age.
Conclusion: Despite growth retardation the difference in height between the sexes is the same as that found in healthy individuals. Even though puberty appears somewhat early, the charts show that DS individuals have a decreased pubertal growth rate. Our growth charts show that European boys with DS are taller than corresponding American boys, whereas European girls with DS, although being lighter, have similar height to corresponding American girls.

Down's syndrome (DS) is the most common chromosomal disorder, with an incidence of about 1/800 live births in Sweden.[1 2] It is associated with mental retardation and congenital malformations, especially of the heart.[3] DS is also characterised by dysfunction/disease in several other organs.[4 5]

Short stature is a cardinal feature of DS.[6] The growth retardation of children with DS commences prenatally.[7] After birth growth velocity is most reduced between 6 months and 3 years of age.[6 8] Puberty generally occurs somewhat early and is associated with an impaired growth spurt.[6 9]

Statural growth is a well known indicator of health during childhood. As growth and final height differ markedly between children with DS and healthy children, standard growth charts should not be used for children with DS. If the growth of a child with DS is plotted on a standard growth chart, the development of an additional disease, such as hypothyroidism or coeliac disease, may be overlooked.

Several syndrome specific growth charts have been developed.[6 10–15] Previously published growth charts for DS are based on American,[6 10] Sicilian,[11] and Dutch[12] populations. The American DS growth charts[6] are frequently used all over the world. As we have shown earlier that the mean final height of Swedish boys with DS exceeds that of corresponding American boys,[9] and as the reported difference in final height between the American boys and girls was low,[6] there was a need for new DS growth charts. Thus, the aim of this study was to create growth charts for Swedish children with DS and to compare these with the presently used DS growth charts of Cronk and colleagues[6] and the Swedish standard growth charts of Karlberg and colleagues.[16]

MATERIALS AND METHODS

The study is based on data from 4832 examinations of 354 children and young adolescents with DS, 57% males and 43% females. The children were born between 1970 and 1997. Data from 203 children (120 males, 83 females) with DS were collected from records on all individuals with DS of four different paediatric units in Sweden (Uppsala University Children's Hospital, Danderyd Central Hospital, Eskilstuna Central Hospital, and the Halmstad County Hospital). Another set of data was obtained from 151 children (83 males, 68 females) with DS, whose parents responded to an appeal in a journal for parents of mentally handicapped children. The only children who were excluded were 10 patients who had earlier been treated with growth hormone within a study. Thus, all other children, regardless of complicating disease such as congenital heart defect and hypothyroidism, were included. The number of observations per child differed somewhat between the two groups (table 1), but there was no observed difference between the groups in parameters related to growth. The majority of the children were white and were born in Sweden.

Table 1 Distribution of the number of children and the number of observations for the two groups of Swedish children with Down's syndrome

	Group 1	Group 2	Total
Males			
No. of children	120	83	203
No. of observations	1363	540	1903
Females			
No. of children	83	68	151
No. of observations	956	571	1527

Group 1: all children living in specified regions of Sweden.
Group 2: children with Down's syndrome recruited from an appeal.

The data used for creation of the growth charts were age at examination (years and months), height (cm), weight (kg), and head circumference (cm). Body mass index (BMI, kg/m^2) was also calculated. The growth charts cover the time period

Abbreviations: BMI, body mass index; DS, Down's syndrome

Table 2 Sample size groupings of the analysed males and females with Down's syndrome

Males											
Age (months)	0	1	2	3	4	5	6	7	8	9	10
No. of observations	*120*	*76*	*68*	*57*	*50*	*55*	*49*	*50*	*38*	*43*	*43*
Age (months)	11	12	13	14	15	16	17	18	19	20	21
No. of observations	*41*	*48*	*25*	*38*	*26*	*35*	*24*	*20*	*22*	*26*	*16*
Age (months)	22	23	24–26	27–29	30–32	33–35					
No. of observations	*15*	*19*	*63*	*56*	*45*	*44*					
Age (years)	3	4	5	6	7	8	9	10	11	12	13
No. of observations	*99*	*81*	*47*	*47*	*41*	*46*	*38*	*35*	*34*	*29*	*23*
Age (years)	14	15	16	17	18						
No. of observations	*45*	*35*	*30*	*30*	*35*						
Females											
Age (months)	0	1	2	3	4	5	6	7	8	9	10
No. of observations	*90*	*50*	*48*	*53*	*41*	*39*	*51*	*32*	*31*	*39*	*33*
Age (months)	11	12	13	14	15	16	17	18	19	20	21
No. of observations	*22*	*55*	*18*	*20*	*17*	*20*	*10*	*40*	*15*	*13*	*18*
Age (months)	22	23	24–26	27–29	30–32	33–35					
No. of observations	*13*	*13*	*37*	*26*	*31*	*19*					
Age (years)	3	4	5	6	7	8	9	10	11	12	13
No. of observations	*61*	*56*	*45*	*41*	*57*	*47*	*47*	*50*	*42*	*38*	*47*
Age (years)	14	15	16	17	18						
No. of observations	*45*	*44*	*29*	*29*	*37*						

from birth until 18 years of age, except those for head circumference, which cover the first four years of life.

The data for each sex were divided into 44 different age groups, one month intervals during the first two years of life, three months intervals during the third year of life, and one year intervals thereafter (table 2). Each child contributed only one single set of data for each age group. If data from more than one examination within an interval were available, the figures from the first examination were used.

The growth charts were compared with those presently used for children with DS, based on American children in studies by Cronk and colleagues[6] (height and weight) and Palmer and colleagues[10] (head circumference). A comparison was also made with the Swedish standard growth charts for healthy children according to Karlberg and colleagues,[16] which correspond well to those of National Center for Health Statistics (NCHS).[17]

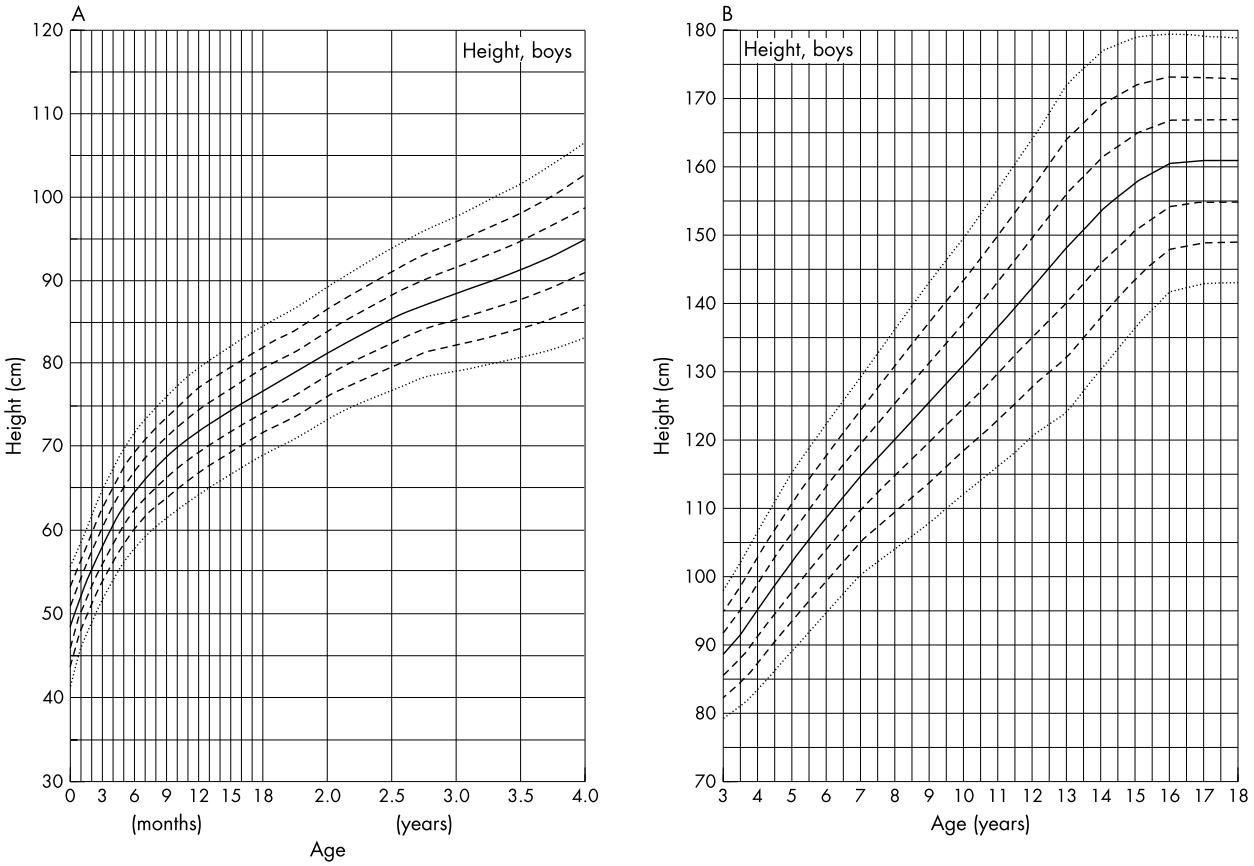

Figure 1 Growth charts for height (mean (SDS)) of boys with Down's syndrome from birth to 4 years of age (A) and 3 to 18 years of age (B).

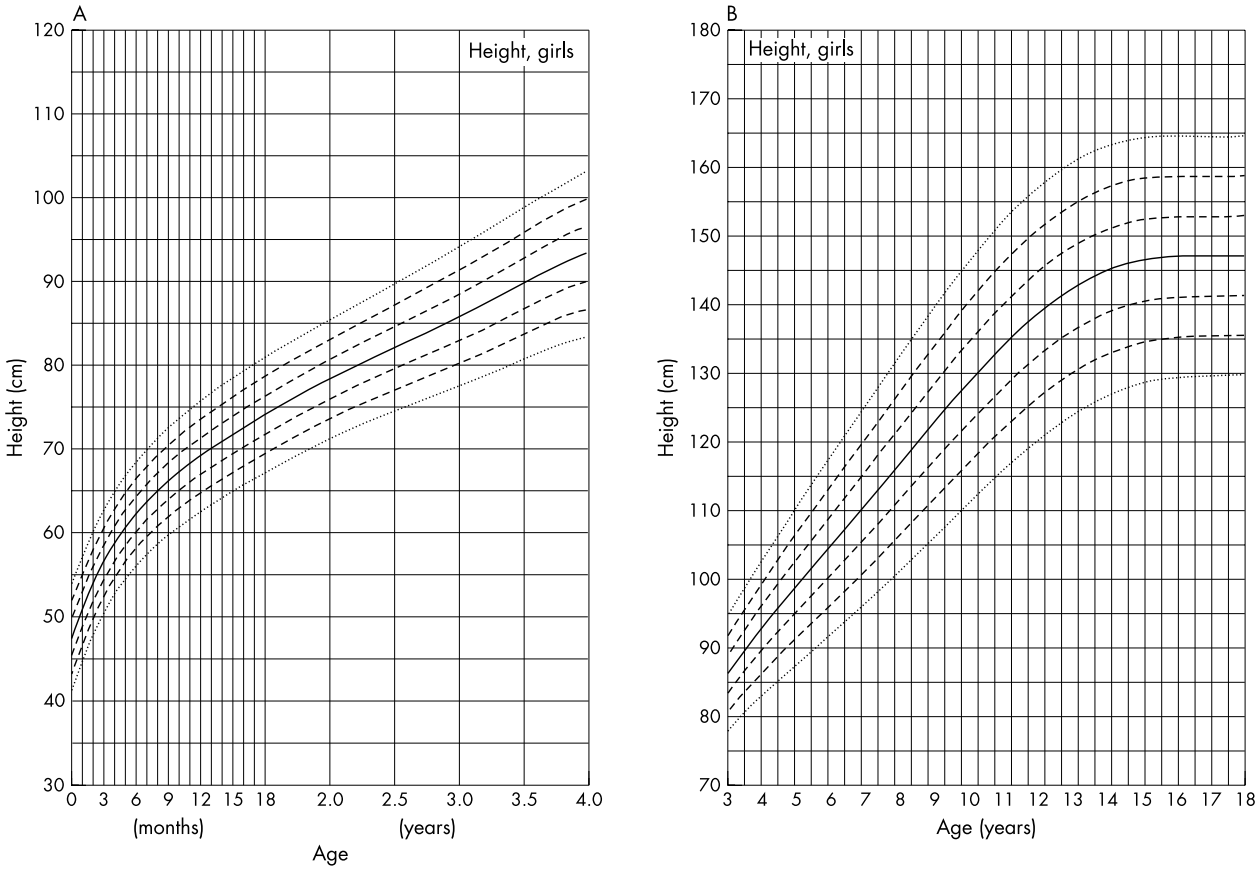

Figure 2 Growth charts for height (mean (SDS)) of girls with Down's syndrome from birth to 4 years of age (A) and 3 to 18 years of age (B).

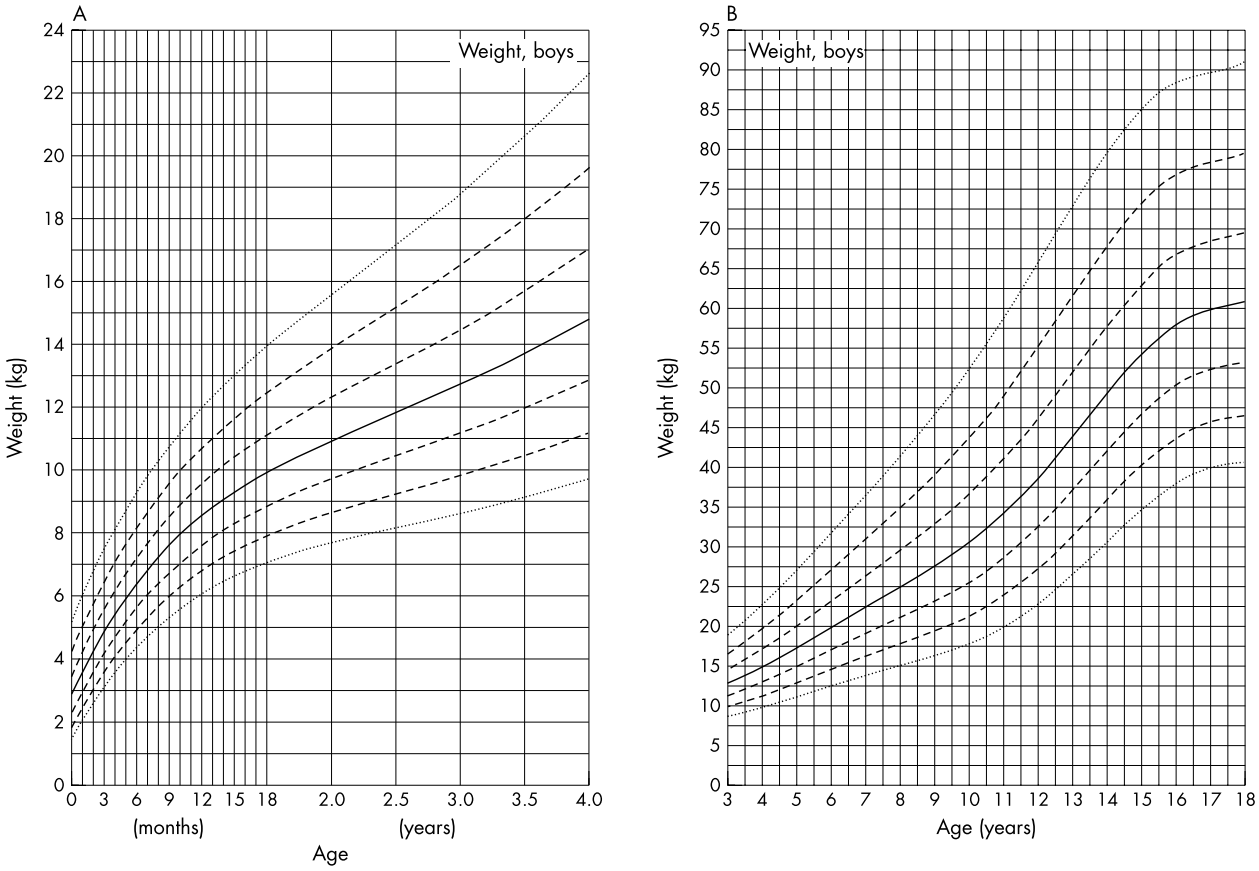

Figure 3 Growth charts for weight (mean (SDS)) of boys with Down's syndrome from birth to 4 years of age (A) and 3 to 18 years of age (B).

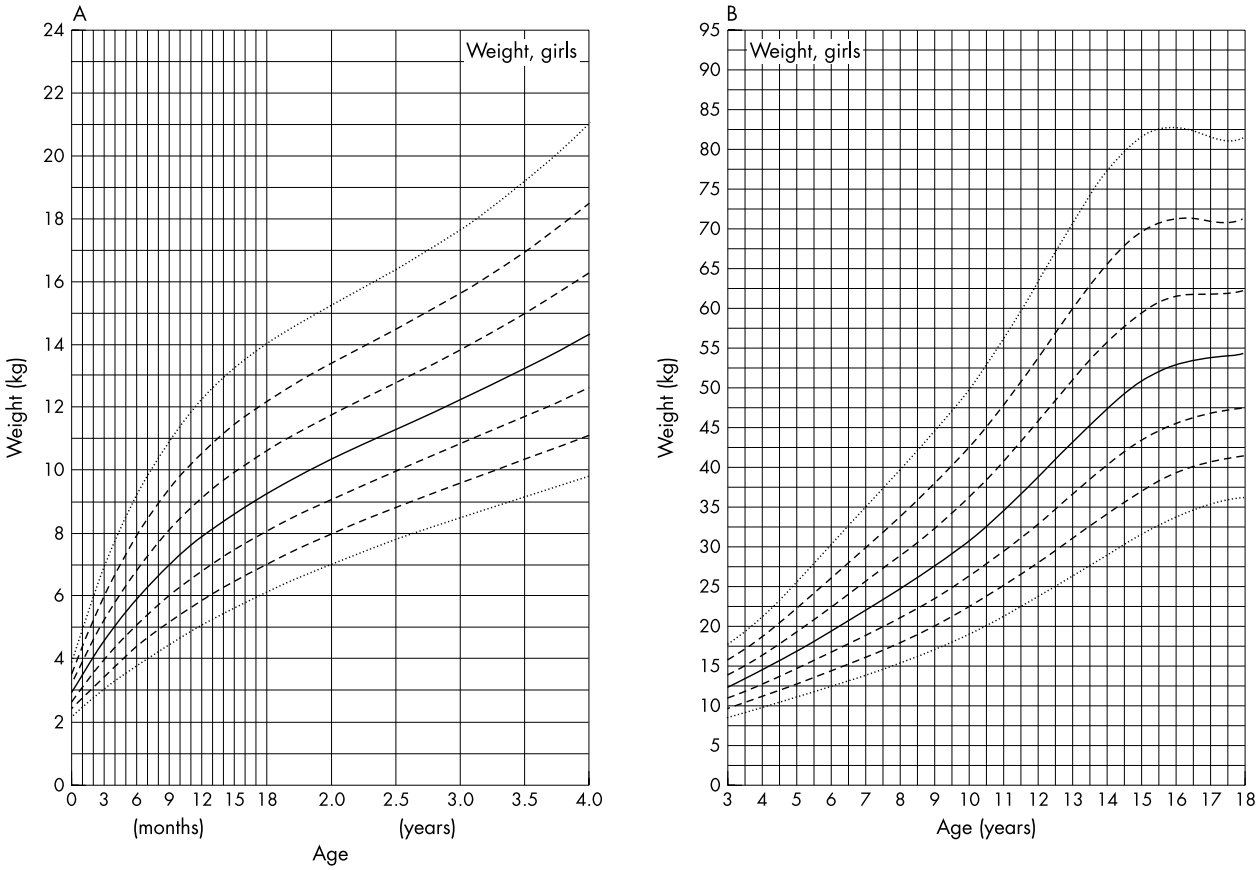

Figure 4 Growth charts for weight (mean (SDS)) of girls with Down's syndrome from birth to 4 years of age (A) and 3 to 18 years of age (B).

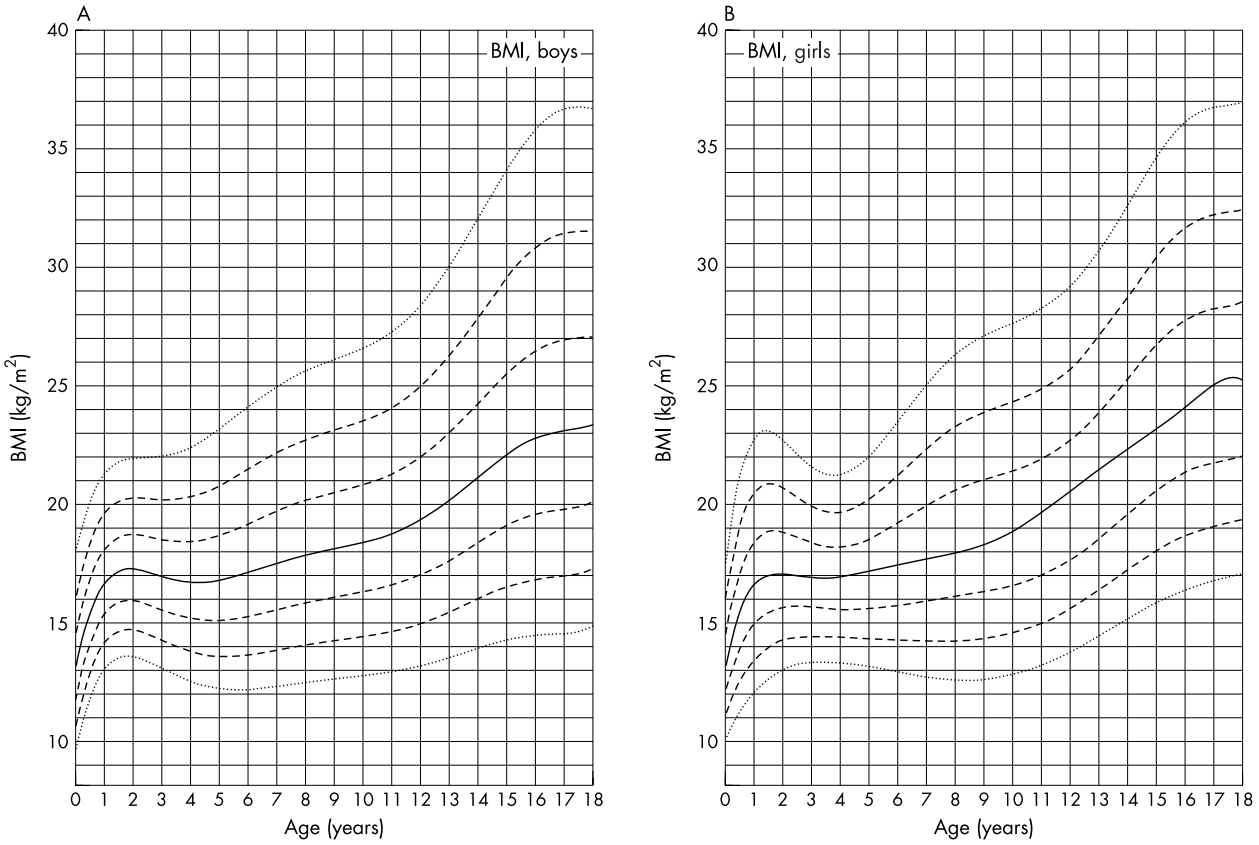

Figure 5 Mean BMI of boys (A) and girls (B) with Down's syndrome from birth to 18 years of age.

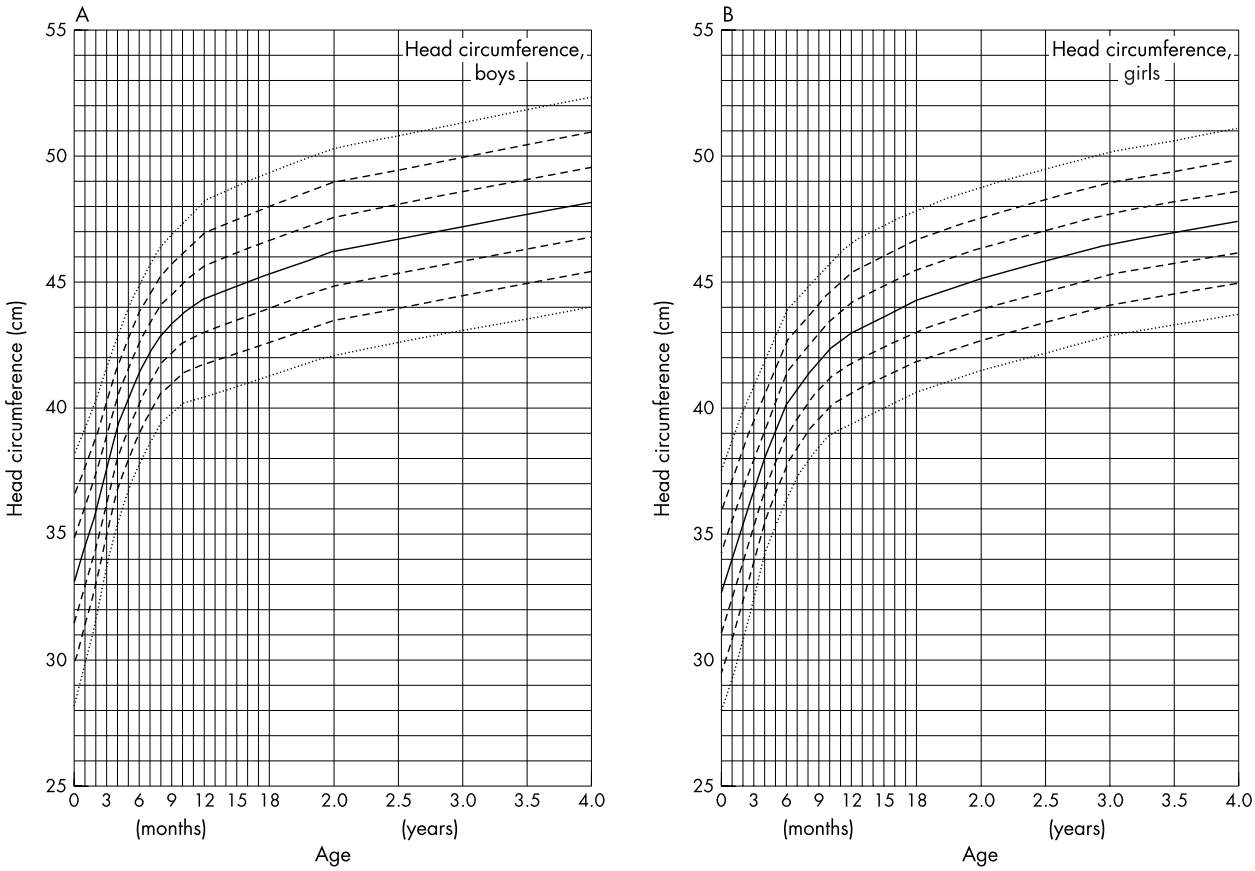

Figure 6 Growth charts for head circumference (mean (SDS)) of boys (A) and girls (B) with Down's syndrome from birth to 4 years of age.

Data for weight and BMI were transformed into logarithms before the statistical analysis in order to obtain normal distributions. All growth charts are based on means and standard deviations using the weighted regression fitness system distributed by Jandel.[18] The software used was Microsoft Excel 97 SR-1 (Microsoft Corporation, Redmond, WA, USA) and SigmaPlot, Scientific Graph System, version 3 for Windows (Jandel Scientific Software, San Rafael, CA, USA).

RESULTS

Figures 1 and 2 present growth charts for height for boys and girls. Mean birth lengths of both boys and girls with DS were 48 (2.3) cm (figs 1A and 2A), corresponding to −1.5 SD and −1 SD, respectively, on growth charts for healthy Swedish children.[16]

The mean final height of males with DS (fig 1B) was 161.5 (6.2) cm (−2.5 SD, Swedish standard[16]) and that of females with DS (fig 2B) 147.5 (5.7) cm (−2.5 SD[16]), resulting in a difference of 14 cm between the genders. The mean final heights, when plotted on the growth charts of American children with DS,[6] were on the 95th and slightly above the 50th centiles, respectively. Individuals with DS reached their final height at relatively young ages, 16 years for males and 15 years for females (fig 1B and 2B).

Figures 3 and 4 show the charts for weight. The boys had a mean birth weight of 3.0 (0.6) kg (fig 3A) corresponding to −1.2 SD.[16] The mean weight at 18 years of age was 61 (8.3) kg (fig 3B) corresponding to −0.4 SD according to the Swedish standard[16] and the 55th centile of American DS growth charts.[6] Corresponding figures for females with DS were 2.9 (0.3) kg (−1.5 SD[16]) and 54 (7.5) kg (−0.5 SD[16] and 25th centile[6]), respectively (fig 4A and B). A body mass index (BMI) above 25 kg/m^2 was observed in 31% of the boys and 36% of the females at 18 years of age (fig 5A and B).

Figures 6A and B show the increase in head circumference. At birth, the boys had a mean head circumference averaging 33.0 (1.7) cm, corresponding to −0.5 SD, whereas that at 4 years of age was 48 (1.4) cm, −2.0 SD, Swedish standard.[16] The head circumference of the girls with DS developed in a similar way with means of 32.5 (1.6) cm at birth and 47.5 (1.2) cm at 4 years of age corresponding to −0.7 SD and −2.0 SD,[16] respectively.

DISCUSSION

Syndrome specific growth charts have been developed for several different disorders, for example, Down's syndrome,[6 10–12] Turner syndrome,[13] Noonan syndrome,[14] and Prader–Willi syndrome.[15] These charts are important tools in the medical care of these children. Short stature is a cardinal sign of Down's syndrome. Complicating disorders, such as coeliac disease, hypothyroidism, and growth hormone deficiency may aggravate the growth retardation. For detection of additional growth deviation the use of growth charts specific for children with DS are necessary. In this investigation we present growth charts from birth to 18 years of age for children with DS.

The growth pattern is characterised by an impaired growth velocity from birth until adolescence, especially during the age interval of 6 months to 3 years and during puberty. In comparison with healthy boys, the males with DS had mean birth length and final height at 18 years of age corresponding to −1.5 SD and −2.5 SD,[16] respectively. When the present data were compared to the American DS growth charts[6] the final height corresponds to the 95th centile. The rather marked difference in final height between Swedish and American males with DS cannot be explained at present, but may be caused by factors such as ethnic diversity and differences in size of the study groups.

The girls with DS in the present study had a mean birth length of −1 SD and a mean final height, at the age of 18 years, of −2.5 SD according to the Swedish standard.[16] The final height of the girls with DS was slightly greater than that of the American girls. Birth lengths for our children with DS could not be compared with those of the Americans, as the latter growth charts start at 1 month of age.

The individuals with DS reached their final height at relatively young ages, 16 years for males and 15 years for females. This is in agreement with earlier studies in which an early onset of puberty has been reported.[6 8 9] Our results also show that individuals with DS have a reduced pubertal growth spurt, contributing to the low final height. In contrast to the American data[6] our individuals with DS had the same difference in mean final height between the genders as healthy individuals.

Certain groups, in which mental retardation is predominant, such as the Prader–Willi and Bardet–Biedl syndromes, are predisposed to overweight.[19] Despite having a greater mean final height than their American counterparts, the mean weight at 18 years among the Swedish males with DS was close to the 50th centile of the corresponding American males. The mean weight for Swedish girls with DS was at the 25th centile of the American growth charts[6] at the age of 18 years. Even though one third of the individuals with DS were overweight (BMI >25 kg/m^2), as defined by the National Institute of Health (NIH),[20] at the age of 18 years the weight and height data of the American individuals with DS indicate that overweight is a greater problem in the latter group.

Considering the mental retardation associated with DS the growth of the head is of great interest. Our results show that the mean head circumference of the children with DS was smaller than that of healthy Swedish children, but slightly greater than that of American children with DS. In agreement with previous studies there was a gender difference in head circumference, the male head tending to be larger than the female.[10 11]

Although the optimal choice for the creation of growth charts would be a longitudinal, prospective study based on repeated examinations of a large and representative group, the drawbacks with respect to time constraints and logistics make it a less attractive model. Another way of collecting data is by multiple and detached examinations at separate ages, but given 354 children and 4823 examinations such an analysis would produce less than 15 sets of data in each group which would not result in reliable growth charts. In the present study we used both repeated data for each child, as in a longitudinal study, and several examinations of different children in the same age group, as in a cross sectional study. This is a common solution when growth in specific groups with relatively few subjects is analysed.[6 12 21 22]

No children were excluded from the present study as a result of additional disorders. Thus, treated hypothyroidism and coeliac disease should not affect growth to any significant extent. Congenital heart defects may affect growth, but are part of the syndrome for 50% of the DS population.[23] It has been shown that differences in mean stature, comparing those without or with mild congenital heart disease and those with moderate or severe heart disease, are no greater than 2 cm for boys and approximately 1.5 cm for girls up until the age of 8 years. The corresponding difference in weight varies between 0.5 and 2 kg.[6]

To make certain that there was no bias in the selection of the children in the study, the mean scores and standard deviations of all parameters were compared between the two groups of children recruited. There were no differences in any of the parameters related to growth in the children included by the appeal compared to those from the four paediatric units.

Since it is not possible to switch from measurement of supine to standing height at a fixed age in children with DS there is no gap in height at the age of 2 years as in Swedish standards for healthy children.[16] Only a slight irregularity in the curve between 2 and 4 years of age was observed.

In the present work we do not report comparisons between our DS growth charts and the corresponding Dutch and Sicilian growth charts. The Sicilian growth charts are based on a rather small number of children and cover only the period up to 14 years of age. The Dutch growth charts for children with DS are similar to our charts, but are based on less than half the number of examinations.

Prader–Willi syndrome and DS share many features related to growth. No differences can be shown during the prepubertal period comparing syndrome specific growth charts for the two.[24] A beneficial effect of growth hormone therapy is well established in Prader–Willi syndrome[25] and may also be of significance in treatment of children with DS.[24 26–28]

Growth is an excellent marker of health status, both on an individual and population level. This is especially evident in disorders such as DS, which is associated with the dysfunction of several organ systems. Short stature is a characteristic feature of DS, but there is a pronounced individual variation. This variation is influenced both by genetic factors from the extra chromosome 21 and inherited parental factors. In addition concomitant diseases may influence growth. Children with DS are great consumers of health care and are seen by many different physicians. Growth charts specific for children with DS are therefore important tools in the medical routine follow up as well as in the monitoring of growth promoting treatments.

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ARCHIVIST

Epidemiology of birthweight

Babies with lower birthweights have higher risks of dying in infancy. Populations with lower mean birthweights usually have higher infant mortality rates. So is low birthweight, of itself, an adequate explanation of increased infant mortality? It has been argued that it is not (Allen J Wilcox. *International Journal of Epidemiology* 2001;**30**:1233–41).

If you plot neonatal mortality (y-axis, logarithmic) against birthweight (x-axis) you get a reversed J-curve with neonatal mortality falling from a very high level at very low birthweights to a minimum at about 3.5 kg (US data) and then increasing again at higher birthweights. (Optimal birthweight tends to be somewhat higher than mean birthweight.) Changing circumstances tend to change the level but not the shape of the curve. Thus, in the USA neonatal mortality fell for all birthweights between 1950 and 1988 so the 1998 curve lies below but parallel to the 1950 curve. (There is, incidentally, no change in the curve at 2.5 kg so the distinction between low birthweight and normal birthweight is arbitrary). Factors, such as maternal smoking or high altitude residence, which reduce birthweight in populations simply shift the reversed-J to the left. This produces the "low birthweight paradox" because low birthweight babies in the reduced-birthweight group then have lower mortality rates than babies of the same birthweight in the standard group. Maternal smoking then appears to be "beneficial" for lower birthweight babies. Wilcox solves the paradox by plotting neonatal mortality against birthweight z-scores for each group. It is then found that the neonatal mortality of babies of smoking mothers exceeds that of babies of non-smoking mothers at all points of the curve. Therefore, maternal smoking reduces birthweight at all levels but the effect on neonatal mortality is independent of birthweight. Wilcox argues that attention should be focussed on preterm births either by recording of gestational age or by estimation of the proportion of small preterm births from the "residual distribution" of the birthweight frequency distribution. (The "residual" distribution is the lower tail lying outside the normal, bell-shaped, curve and is almost entirely due to small preterm births.)

Two commentators (Ibid: 1241–3 and 1243–4) accept that the low birthweight/normal birthweight dichotomy is outdated but challenge Wilcox's conclusions, one because he believes that Wilcox takes too little heed of the social context and the other because she still believes that birthweight can be informative about population health.