f. *Chronic diseases:* Many chronic diseases can retard growth. Notable among them are asthma, hemolytic anemias, congenital heart disease, malabsorption states, renal tubular acidosis and renal failure. GH levels are normal, and often elevated in these disorders. However, IGF-I (insulin like growth factor-I) levels tend to be low in these situations. It is worthwhile to point here that GH exerts its growth promoting effects primarily through generation of IGF-I.

g. *Growth variation in response to physiological needs:* Alaskans (Tundra) are shorter, stockier, bulkier in physique with shorter appendages. This is because diversion of nutrients from growth to heat production stunts their growth. They also have wider and larger skulls to mitigate heat loss.

h. *Ethnic growth variations:* Variations in growth are observed among different populations. While average height and weight of pre-adolescent well-to-do children tend to be similar, clear ethnic differences appear during adolescence. Thus, Indian and other Asian children who are at 50th centile of NCHS and the recent WHO[12] Standard till 5 years of age, become close to the 25th centile at the end of adolescence. Thus, the WHO recommends that NCHS standards should not be used to evaluate growth of Asian children beyond 10 years of age. Instead, local standards derived from well-nourished children should be used for growth comparison. For India, standards derived by Agarwal et al[9, 13, 14] are suitable. The NCHS—WHO standards are however needed for comparison of nutritional status among different populations across the world. WHO in April, 2006 (Study period 1997–2003)[12] generated longitudinal growth data from birth to 24 months and a cross sectional data on children aged 18 to 71 months. The data were collected from Brazil, Ghana, India, Norway, Oman and USA by selecting healthy children living under conditions likely to favor the achievement of their full genetic potential. However, in view of ethnic and geographical differences WHO standards[12] are debated recently[15, 19] in favor of local standards.

REGULATION OF GROWTH

Glands and growth. The regulators of growth are the Endocrine glands, they are subject to hereditary influence. The pituitary gland secretes growth hormone, which controls general body growth, particularly the growth of the skeleton, and also influences metabolism. In addition to influencing growth directly, the pituitary gland has a central role in regulating the other endocrine glands. These other glands in turn control many body functions, and they secrete the various hormones that directly regulate metabolism.

a. *Infancy:* Growth in various phases of life is regulated by different mechanisms.

   From 20 wk of gestation to six months postnatally the growth is primarily under the control of brain / hypothalamus and is nutrition dependent.

b. *Childhood:* Six months of age until the prepubertal period, GH (growth hormone) and thyroxine are the key hormones controlling growth. The childhood component of growth adds about 70 cm to height.

   During late childhood adrenal androgens also influence growth, particularly in boys—**Adrenarche**

c. *Adolescence:* Pubertal growth is regulated by both GH and sex hormones. Thyroxine continues to play an important role in pubertal growth.

Variations in growth rates: The growth of different individuals varies a great deal. It should be remembered that the rate of

above and below the target height 97th and 3rd centiles are constructed by tracing lines backwards to match the current age. If the projected and target height differ by more than 5 cm, then child need to be evaluated for pathological causes of short stature.

To summarize

- This height prediction is based on the sex adjusted midparental height:
  - *For girls:* Subtract 13 cm from the father's height and average with the mother's height.
  - *For boys:* Add 13 cm to the mother's height and average with the father's height.
- 13 cm is the average difference in height of women and men.
- For both girls and boys, 8.5 cm on either side of this calculated value (target height) represents the 3rd to 97th percentiles for anticipated adult height.
- Thus, a child's genetic potential for height is expressed by the mid-parental height (*see* page 6)

When to Worry in Growth Variations/Faltering?

(i) First three years

- Length/height, weight or head circumference below 3rd percentile or above 97th percentile on growth chart.
- Crossing of two major percentile lines (upward or downward), e.g. going from above 75th percentile to below 50th percentile on height or weight chart.
- A child below or above mid-parental range for height/length
- Weight loss or lack of weight gain for a month in the first 6 months.
- Absence of weight gain for 2–3 months from 6 to 12 months of age.
- Micropenis.
- Unilateral or bilateral undescended testis.
- Ambiguous genitals.

(ii) Three to nine years

- Length/height below 3rd percentile or above 97th percentile on growth chart.
- Crossing of two major percentile lines (upward or downward), e.g. going from above 75th percentile to below 50th percentile on height or weight chart.
- A child below by 5 cm mid-parental range for height.
- BMI over the 85th percentile at all ages.
- Rate of growth less than 5 cm/year.
- Girls with axillary, pubic hair growth or breast budding before 8 years and boys with axillary, pubic hair growth, genital growth or and testicular enlargement before 9 years.
- Children with craniospinal irradiation or surgery for brain tumors.
- Micropenis.

(iii) Nine to eighteen years

- Height below 3rd percentile or above 97th percentile on growth chart.
- Crossing of two major percentile lines (upward or downward), e.g. going from above 75th percentile to below 50th percentile on height or weight chart.
- A child below or above mid-parental range for height.
- BMI over the 85th percentile at all ages.
- Arrest at the same stage of puberty for more than 2 years.
- Micropenis.
- Unilateral or bilateral gynecomastia in boys.
- Hirsutism and menstrual irregularities in girls.
- Delayed puberty that is girls with no breast budding by 14 years or no menarche by 15 years and boys with no signs of puberty by 16 years.

Clinical Interpretation of Anthropometric Data

Please *see* Chapter 4, and Table 1.5.

instead of MGRS. Weight and head circumference varied more than the height.

The study concluded that height and weight may not be the optimal fits in all cases; similarly **MGRS head circumference means may put many children at risk of misdiagnosis of micro/macrocephaly**. The study recommended that country reference data may be more ideal for assessing growth.

Advantages of WHO Charts

Birth to 5 years: Purely breastfed followed by emphasis on breastfed.

Disadvantages of WHO 2007 (Birth to 18 years) Charts

1. It assumes all populations in the world are equally tall. After 5 years, it extends the lines to 18 years statistically based on NCHS charts. The fact is that Indian affluent children of as recent as Khadilkar et al[20] data do not have the same pubertal growth spurt as do Americans, and our final height is shorter.
2. BMI centiles at 18 years are heavier than prescribed BMI for adult Indian cut-off.

What have Other Countries done?

1. *USA:* Felt from 1977 (1 year after 1976 NCHS charts were made) that there were some inaccuracies in the NCHS charts, mainly pertaining to head circumference data of birth to 5 years, as well as preterm data, and statistical smoothening procedures. They convened many workshops, which resulted in the CDC 2000 charts. While making the CDC charts, they **excluded weight data of NHANES III**, on the grounds that the children had become too heavy and that misclassification of obesity and overweight would occur.
2. *UK:* Felt on account of breastfed, and preterm representation, should adopt WHO standards and they made UK–WHO 2009 charts in May 2009. This is **only for birth to 4 years**. For 4 to 18 years, UK 90 charts are still continued to be used.

In recent years two more studies have appeared one being multicenter by Khadilkar et al[20] and second from Delhi schools by Marwah et al.[21] The distribution of study subjects is shown below with comments.

Khadilkar et al[20] data is more skewed towards right side. It has more extreme values on the right of the median as compared to Agarwal et al[9, 13] data. Figure shows that Khadilkar et al data have more dispersion in comparison to Agarwal et al[9, 13] data (Figs 1.15 a to d).

The density curves comparing primary data dispersion of Agarwal et al[9, 13] and Marwah et al[21] data are closer (Fig. 1.16).

Khadilkar et al[20] data line for 3rd centile flattens after 14 years of age (skewing); as compared to Agarwal et al[9, 13] and Marwah et al[21] (Fig. 1.17).

1. Further comparing Agarwal et al[9, 13] school data (ICMR) against recently available Khadilkar et al[20] data are important in that they take a look at secular trend in height and weight over the last 20 years among children from affluent families having no constraints to nutrition and health. They found no increase in final height at 18 years at the 3rd centile; only 0.6 cm increase in boys at 50th centile, and 1.7 cm (in boys) to 2 cm (in girls) increase in height at the 97th centile.
2. For weight, the 50th centile boys were 2.9 kg heavier at 18 years and 97th centile were 14.7 kg heavier. For girls, the respective figures were 8.0 kg at 17 years.

For BMI, Khadilkar et al[20] 85th and 95th centiles were 26.2 and 30.3 kg/m^2 in boys and 25.9 and 29.9 kg/m^2 in girls. Agarwal et al[13] 85th and 95th for boys were 23.6 and 28, and for girls 23.0 and 25.9 at 17 years. The adult cut-offs recommended for overweight and obesity in Indians are 23 and 28 kg/m^2.

SUMMARY

Puberty–Girls

1. First sign of ovarian estradiol secretion is breast development "Thelarche". SMR-B_2 (breast budding)—Growth in height.
2. Estradiol is a good stimulator of "GH" it doubles the growth velocity 'peak height velocity' (9–10 cm / yr). Coincides with B_3 follows B_2 by 1 year.
3. Change in body shape
4. Growth under arm hair followed by secretion
5. Menarche follows PHV by 14–18 months
6. Adult size breast

Normal Male Development

Sexual development in boys: Testicular enlargement usually occurs between ages of 12 and 13 years. The pre-pubertal testes are about 2 ml in volume, with puberty taken to begin when a volume of around 4 ml is attained. Testicular growth starts as early as 10 years of age, associated with enlargement of seminiferous tubules, epididymis, seminal vesicles and prostate.

Penile and scrotal enlargement occurs typically about a year after testicular enlargement. Pubic hair typically appear at a similar time (Appendix Tables 22 and 23, Indian affluent boys).

The growth spurt occurs later than in girls, possibly because testosterone is less of a stimulus to growth hormone responsiveness than estradiol in girls and is required in relatively higher concentrations of testosterone to produce the same anabolic effect. A greater and later growth spurt occurs in boys and ultimately achieves an average 12–13 cm greater height in adult men than the female counterparts. The growth spurt is on an average 2 year later than girls thus boys get 2 year extra height gain of 10–12 cm (5–6 cm per year). Although boys are on average 2 cm shorter than girls before puberty begins, finally adult men are on average about 13 cm (5.2 inches) taller than women. Most of this sex difference in adult heights is attributable to a later onset of the growth spurt and a slower progression to completion, a direct result of the later rise and lower adult male levels of estradiol.

SUMMARY

Puberty—Boys

1. Adrenarche is the onset and continuity of male puberty
2. Testosterone / dihydrotestosterone are needed in large concentration to initiate "GH" via the androgen receptors. (Thus, later than girls by 1–2 year)
3. Initiation testicular volume >4 ml; maximum growth "PHV" (10–11 cm / year) attained at testicular volume 10–12 ml (during SMR-G3–4)
4. Testosterone—deepens the voice and increases body muscle mass (lean body mass)

Table 2.1: *Development of breast and pubic hair in girls (see fig. 2.1)*

SMR	*Breast (mean ages)**	*Pubic hair*
1.	Pre-adolescent	Pre-adolescent
2.	Bud stage and papilla elevated as small mound, areolar diameter increased (10.2 yr)	Sparse lightly pigmented straight, medial border of labia (in 22%)
3.	Areola enlarged (11.6 yr) no contour separation	Darker, beginning to curl, increase in amount (in 92%)
4.	Areola and papilla form secondary mound (13.5 yr)	Coarse curly, abundant but amount less than in adult (98%)
5.	Mature nipple projects, areola part of general breast contour (15.6 yr)	Adult feminine triangle spread to medial surface of thigh.

Terms used—thelarche—breast development, adrenarche—pubic hair, axillary hair growth, menarche—first menstrual period. Values in parentheses are mean age of appearance.

*% appearance and mean ages are for Indian affluent children (Indian Pediatrics 1992, Agarwal et al.)