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Physiologic Growth and Development During Adolescence

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Objectives After completing this article, readers should be able to:

1. Recognize the inherent variability in puberty.
2. Describe the usual sequence of pubertal development in both boys and girls.
3. Describe the pattern of linear growth during puberty.
4. Identify pubertal abnormalities that require further evaluation.

Introduction

Adolescence is a complex and dynamic process characterized by simultaneous but asynchronous development within several development streams. These streams include physical development (puberty), cognitive and psychological development, and social development. Although puberty is only one component of adolescent development, it generally is considered to define the onset of adolescence and certainly is the most visible and tangible of all of the developmental changes occurring during this period. This article reviews the physiologic changes associated with normal puberty. Other developmental aspects are not considered here, and the many abnormalities of puberty that sometimes can occur are not discussed in detail.

One of the hallmarks of puberty is its variability. The onset, timing, tempo, and magnitude of pubertal changes are influenced significantly by genetic factors as well as by general health and nutritional, environmental, and socioeconomic factors. The timing of pubertal milestones approximates a normal distribution. Studies correlating the timing of puberty between mothers and children or between twins support a strong genetic influence that has been estimated to account for 50% to 80% of the variance in the timing of pubertal onset. Racial and ethnic variations also are seen. For example, the onset of puberty occurs somewhat earlier in African-American children than it does in Caucasian children.

The age of puberty and menarche has declined steadily over the past several generations, attributed to improvements in overall health and nutrition. Several large investigations have documented this secular trend, and it now generally is agreed that puberty often begins at younger ages than are reported in older texts. As a corollary, pubertal onset that once may have been considered precocious now is recognized as being within the range of normal. The lay press has speculated that the ever-decreasing age of puberty, especially in girls, may be related to environmental exposure to estrogens or to hormonal contamination of the food chain. However, recent studies appear to demonstrate that the trend to earlier puberty has plateaued.

Physiologic Mechanism of Puberty

Although the mechanism of puberty largely has been elucidated, it remains unknown *why* puberty begins when it does in any individual. Body clocks, presumably controlled by “master genes,” are the basis of the current hypothesis to explain pubertal onset, but their existence has not yet been proven. Whatever the signal for puberty to begin, there is broad agreement that it originates in the hypothalamus. These central processes are similar in boys and girls; the sexual dimorphism that appears in puberty is driven by the gonadal production of sex steroids—estrogen in girls and testosterone in boys.

Puberty occurs as a result of the activity of the hypothalamic-pituitary-gonadal axis and the production of estrogen and testosterone. This system is very active in early life,

*Editorial Board.

becomes quiescent during childhood, and is reactivated to begin puberty. The system is fully functional at birth, and sensitive assays have demonstrated small pulses of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) even during the quiescent phase of childhood. The relative inactivity of the system during childhood is believed to be the result of inhibitory central feedback that may be mediated by GABAergic neurons or neurons secreting neuropeptide Y.

With the onset of puberty, the central inhibitory feedback is lifted, and the hypothalamic gonadotropin-releasing hormone (GnRH) pulse generator becomes increasingly active. Pulsatile secretion of GnRH begins first nocturnally and later throughout the entire day. Pulsatile GnRH secretion stimulates increasingly pulsatile secretion of FSH and LH from the pituitary gland. Both the frequency and the amplitude of pulses increase. FSH and LH, in turn, stimulate production of sex steroids. In boys, the testes produce testosterone. In girls, the ovaries produce estrogen. The production of sex steroids allows for the development of secondary sexual characteristics, accelerates somatic growth, permits the emergence of fertility, and mediates a wide range of other physiologic effects.

It is accepted that nutritional and metabolic factors influence puberty, and many lines of evidence support the role of nutritional factors in determining pubertal onset. Leptin, a peptide secreted by adipose cells into the general circulation, has emerged as the putative mediator linking nutritional and metabolic status to pubertal development. For example, leptin levels increase during puberty. In animal studies, leptin increases LH pulse frequency and amplitude and can mitigate pubertal delay in underfed animals. It originally was believed that leptin might determine the timing of pubertal onset by signaling nutritional and metabolic adequacy. However, it now appears that the role of leptin is permissive, making it necessary, but not sufficient, for puberty to proceed.

The adolescent growth spurt is linked to pubertal development through pathways that remain unclear. The control of somatic growth during puberty also begins in the hypothalamus, where growth hormone-releasing hormone and somatostatin are produced. The balance of these two hormones, which have opposite effects, stimulates pulsatile production of growth hormone (GH) by the pituitary gland. Local tissues, under the influence of GH, produce somatomedin-C (also known as insulinlike growth factor), which is directly responsible for the growth of somatic tissue.

Height Growth During Puberty

Height growth that averages approximately 6 cm/y occurs continuously and consistently throughout childhood. There is a slight but significant deceleration in height growth immediately preceding puberty. Once puberty begins, however, height velocity increases sharply, reaching its peak in mid-puberty, immediately preceding menarche in girls and spermatarche (appearance of sperm in the seminal fluid) in boys. The mechanism that links this pubertal growth spurt with sexual maturation is poorly understood.

In girls, linear growth accelerates shortly after thelarche (appearance of breast tissue) at a mean age of approximately 10 years. Peak height velocity of 8 cm/y is reached 6 to 12 months prior to menarche at approximately 11.5 years of age. Linear growth decelerates after menarche. Significant growth continues, however, with the average height gain after menarche averaging 7 cm. Girls who menstruate early grow more after menarche (eg, 10 cm for a girl who menstruates at age 10 y). In contrast, girls in whom menarche is delayed grow less once menarche occurs (eg, an average of only 5 cm of height growth among girls whose menarche occurred at age 15 y).

Just as puberty begins later in boys than in girls, so too does the pubertal growth spurt. Once genital development begins, height growth accelerates, reaching its peak velocity of 9 cm/y at approximately age 13.5 years. Thereafter, height velocity decelerates, with growth usually complete several years later. Boys typically begin their growth spurt up to 2 years later than girls, giving them 2 years of additional prepubertal growth. Peak height velocity is greater in boys than in girls, allowing them to grow faster during their height spurt. Finally, the height velocity curve is broader in boys than in girls, reflecting a pubertal growth spurt of longer duration. The combined effects of additional prepubertal growth, greater peak growth, and a longer duration of the pubertal height spurt explain the height advantage that males generally have over females.

A variety of formulas are available to predict adult height based on radiographically determined bone age. However, because height largely is determined genetically, the height potential of healthy children can be estimated by using a formula based on parental heights. For boys, the formula is mean parental height + 6.5 cm; for girls, the formula is the mean parental height - 6.5 cm. Special growth curves are available for specific populations in whom impairments of growth are known, such as individuals who have Turner syndrome.

Plotting growth on appropriate growth curves can aid

in evaluating pubertal growth and estimating growth potential. It is important to recognize that the traditional growth curves available in most pediatricians' offices are based on cross-sectional data. As such, they are useful in providing average ranges for adolescent growth, but they do not reflect the shape of the growth curve accurately for any individual. Traditional growth curves are sufficient for adolescents whose growth is normal, but they are less useful when growth seems to deviate from the norm—either too early/too much or too little/too slow. In these cases, traditional growth curves are not helpful in distinguishing the adolescent who has a pathologic impairment of growth from the adolescent whose growth is simply constitutionally delayed. In these cases, growth curves keyed to sexual maturity and height velocity are much more useful in differentiating adolescents whose apparent growth deficiency requires further evaluation and possible treatment. Bone age tracks with pubertal development more closely than it does with chronologic age. Therefore, because of the inherent variability in pubertal timing, bone age measurements in adolescents may be discordant with chronologic age by as much as 2 years and still be normal.

Sexual Maturation During Puberty

Although significant variability in the onset, timing, tempo, and magnitude of pubertal changes is characteristic, the *progression* through puberty is consistent and predictable. In fact, the sequence of normal pubertal milestones is so dependable that any deviation from the progression should prompt a careful review and may require further evaluation.

The timing of most pubertal events approximates a normal Gaussian distribution, with a standard deviation of approximately 1 year. Thus, using the average age of any pubertal event, the clinician can extrapolate the normal age range for that milestone as the average age \pm 2 years. This simple relationship relieves the clinician of having to memorize all but a few pubertal ages because the rest can be calculated easily. For example, based on an average age of menarche of 12 to 13 years, a postmenarchal 10-year-old is statistically precocious and a 15-year-old who has yet to menstruate is statistically delayed (12 to 13 y \pm 2 years). It cannot be overemphasized, however, that statistical distinctions between “normal” and “abnormal” are purely arbitrary. Most adolescents who experience late puberty have no pathology; they simply are delayed genetically. Similarly, most adolescents who develop early have no specific pathology. Therefore, although an adolescent whose development lies outside of the statistically “normal” range requires

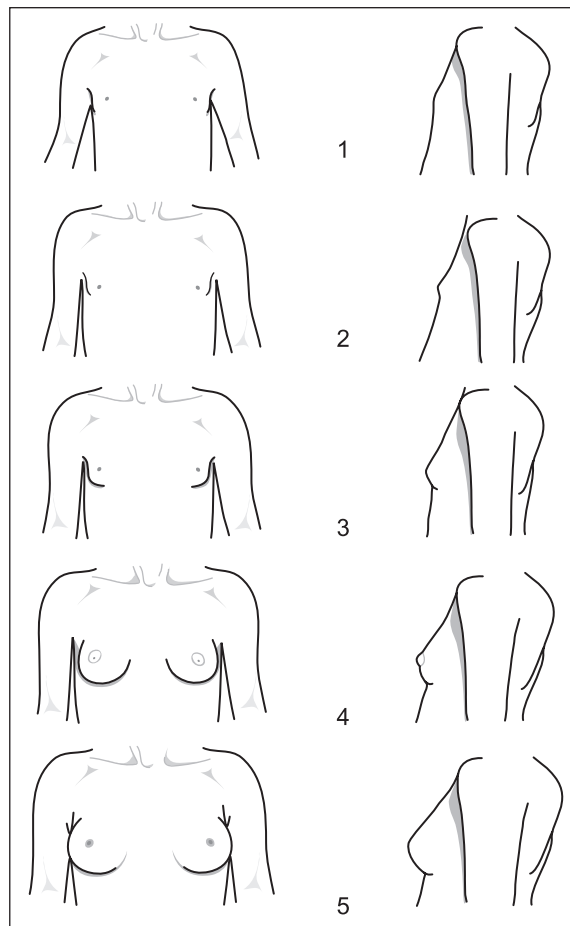


Figure 1. Sexual Maturity Rating for breast development. Stage 1 represents the prepubertal breast in which there is elevation only of the papilla. At stage 2, a “breast bud” forms below the areola. In stage 3, there is further enlargement and elevation of both breast and areola. In stage 4, the areola forms a secondary mound above the contour of the breast. The stage 5 breast is fully mature, with recession of the secondary mound and a smooth breast contour.

clinical evaluation and perhaps laboratory or radiographic investigation, their unusual developmental trajectory likely is due only to the inherent variability in pubertal timing.

Sexual Maturity Rating

The Sexual Maturity Rating (SMR) of Marshall and Tanner typically is used to describe the progression of secondary sexual characteristics that occurs throughout puberty. The development of breasts in girls (Fig. 1) and genitalia in boys (Fig. 2) helps to evaluate the function of the hypothalamic-pituitary-gonadal axis; the development of pubic hair in both boys and girls (Fig. 3) helps to

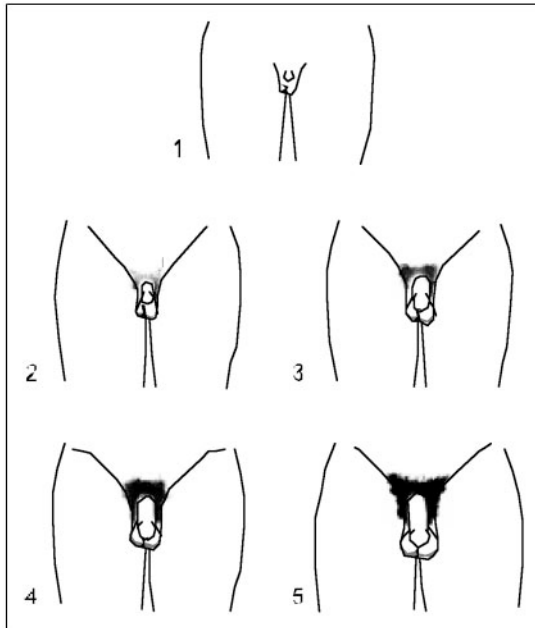


Figure 2. Sexual Maturity Rating for male genitalia. Stage 1 describes prepubertal genitalia. In stage 2, there is enlargement of the testes and scrotum, with reddening and thinning of the scrotum, but no enlargement of the penis. In stage 3, the penis begins to enlarge, first in length and later in diameter. The testes and scrotum continue to enlarge. In stage 4, the testes and scrotum continue to enlarge, with continued lengthening of the penis and enlargement of the glans. Stage 5 represents genitalia of adult size and proportion.

evaluate the function of the hypothalamic-pituitary-adrenal axis. Describing these two axes by using the SMR provides a snapshot of the young person's advancement thorough puberty. At SMR 1, by definition, puberty has not yet begun, and no development has occurred. At SMR 2, development has just barely begun. SMR 3 implies ongoing development; SMR 4 represents development that is nearly complete. By definition, SMR 5 refers to secondary sexual characteristics that are fully developed and adultlike. There often is some asynchrony between the SMRs for breast/genitalia and the SMR for pubic hair, which reflects the slight lag in activation of the hypothalamic-pituitary-adrenal axis once puberty has begun. It also is well-known that the intervals of pubertal development represented by the five SMRs are not equal; the interval represented by SMR 2, for example, tends to be brief compared with the interval represented by SMR 3, which tends to be of much longer duration.

Sexual maturation in girls begins at a skeletal age of approximately 11 years and is summarized in Figure 4. After a prepubertal dip in growth, the visible signs of

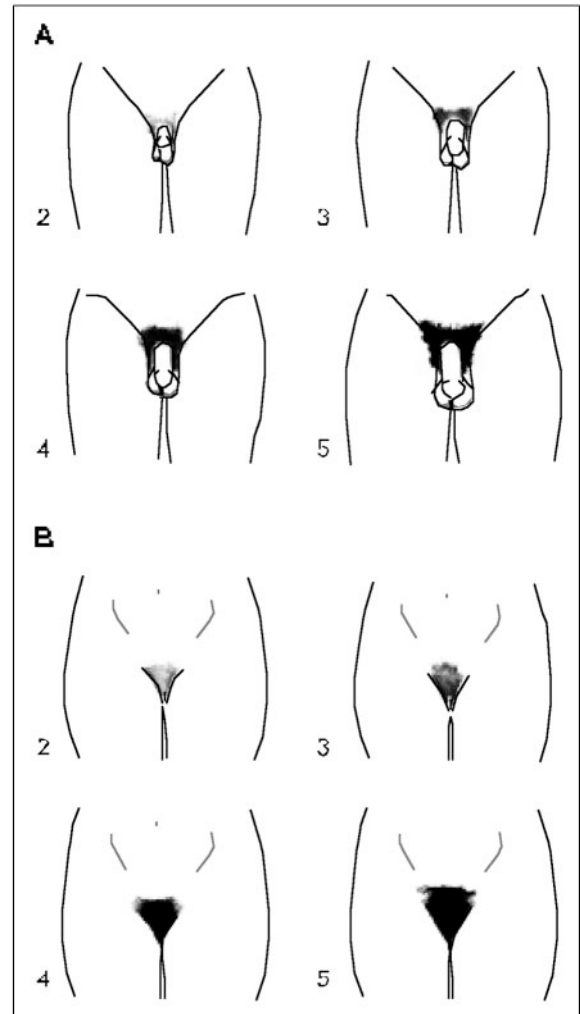


Figure 3. Sexual Maturity Rating for pubic hair. In the prepubertal stage 1, there may be fine vellus hair that is no different from that found over the abdominal wall. In stage 2, there is growth of sparse straight hair, primarily at the base of the penis or along the labia. In stage 3, hair increases in quantity and is darker and curlier. Stage 4 is characterized by pubic hair that resembles adult pubic hair, although the escutcheon covers a smaller area than seen in adults. Finally, in stage 5, pubic hair has increased further in volume, spread onto the medial thighs, and taken on characteristic male or female configuration.

puberty begin with thelarche, which occurs at an average of 10.5 years in Caucasian girls and approximately 1 year earlier in African-American girls. Adrenarche (the appearance of sexual hair) occurs approximately 6 months later, reflecting the subsequent activation of the hypothalamic-pituitary-adrenal axis. The pubertal growth spurt begins shortly thereafter, usually at breast

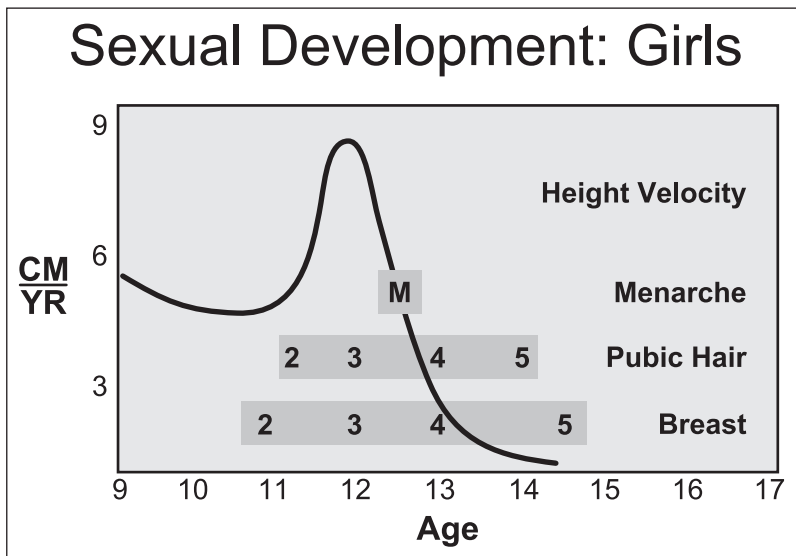


Figure 4. Summary of pubertal development in girls. After a slight deceleration in growth, puberty begins with breast development. Shortly thereafter, pubic hair develops, and linear growth increases sharply. Development of breasts and pubic hair continues, with peak height velocity reached at a mean of 12 years, at SMR 3. Menarche occurs shortly after peak height velocity is attained, usually at SMR 3 to 4. Growth decelerates with menarche, although it continues for some time afterward.

SMR 3. Meanwhile, development of the breasts and sexual hair is ongoing, with a concurrent maturation of the uterus, vagina, and ovaries. The pubertal growth spurt peaks just prior to menarche, which occurs in Caucasian girls at an average age of 12.9 years and in African-American girls at an average age of 12.2 years. Physiologic leukorrhea often appears in the 6 months preceding menarche. By the time menarche occurs, growth velocity is decelerating rapidly, although some growth usually continues until an average skeletal age of 15 years. By this time, pubertal development usually is complete.

In boys, puberty begins nearly 2 years later than in girls, at a skeletal age of approximately 13 years (Fig. 5). Thinning of the scrotum and testicular enlargement, often subtle, are seen first at an average age of 11.5 years. (Testicles that are less than 2.5 mm in length are considered prepubertal.) As in girls, adrenarche occurs approximately 6 months later at an average age of 12 to 12.5 years. The growth spurt follows, but occurs rela-

tively later (at genital SMR 4 in boys versus breast SMR 3 in girls). Development of the genitalia and sexual hair continue. Facial hair, change in voice, and the appearance of sperm in seminal fluid all tend to occur at genital SMR 3 to 4. Gynecomastia (the transient development of breast tissue in boys) affects up to 50% of males and is most prominent at genital SMR 4. In addition to beginning later, pubertal maturation in boys has a slower tempo than in girls. Both generally are complete at a skeletal age of 17 years. Pubertal gynecomastia, as well as normal breast development, can be asymmetric; neither indicates pathology.

Other Physiologic Changes During Puberty

Although sexual maturation and the height spurt are the preeminent pubertal events, many other physiologic changes take place during puberty. The central nervous system grows, and lymphoid tis-

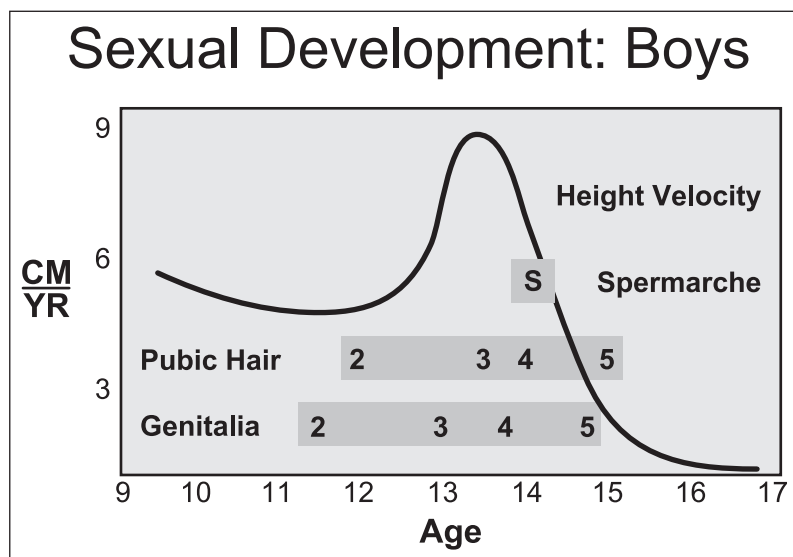


Figure 5. Summary of pubertal development in boys. Pubertal development begins in boys later than in girls. After a gradual deceleration in linear growth, development of the testes and scrotum begins, although it often is unnoticed by boys. Pubic hair develops shortly thereafter, along with acceleration in height growth. Development of the testes, scrotum, and pubic hair continue; the penis also begins to grow. Peak height velocity is reached typically at SMR 4. The shape of the height velocity curve is broader than in girls, with a more gradual decline in growth velocity after the peak of height growth is reached. Spermarche generally occurs at SMR 4. Genitalia and pubic hair may continue to develop for years.

sue regresses significantly. The heart, lungs, and viscera all increase in size and mass. Blood pressure gradually increases, and essential hypertension can begin to appear in susceptible individuals. Gender-specific changes in body composition occur. Although muscle mass and strength increase in both males and females, males become relatively leaner and females become relatively less lean.

Physiologic development also is reflected in age-specific laboratory values. Rapid bone growth generates transient elevations in alkaline phosphatase. Sensitive assays can demonstrate “supranormal” but nevertheless age-appropriate levels of GH and sex steroids. The red blood cell mass increases in both males and females, with boys establishing norms of hemoglobin and hematocrit that are slightly higher than those of girls. Cholesterol levels begin to rise. Serum creatinine levels also rise to reach adult standards.

Clinical Evaluation of Puberty

Evaluation of growth and development is a fundamental undertaking of pediatrics, and this assessment is as important during adolescence as it is during infancy. Ongoing monitoring of growth and development is a useful mirror of overall health, nutrition, and well-being. In its *Bright Futures* guidelines, The American Academy of Pediatrics recommends annual health supervision visits for adolescents as a means to provide comprehensive preventive care, including continuing assessment of growth and development. These visits also allow for the early detection of pubertal dysfunction and provide an opportunity to address other issues of adolescence.

As with many developmental processes, the experience of puberty differs from individual to individual. However, as described previously, the progression through puberty is remarkably consistent and predictable. Significant deviation, such as the appearance of vaginal bleeding before the height spurt, should prompt careful evaluation or prompt referral.

Precocious puberty is much more common in females than in males and usually is related to idiopathic early activation of the hypothalamic-pituitary-gonadal axis. New age limits for defining when puberty is precocious, reflecting younger contemporary norms, have been published for girls. Age limits that define precocious puberty in boys have not changed, and precocious puberty in boys is more likely to be due to a pathologic process.

Pubertal delay is more common in males than in females and recently was reviewed in *Pediatrics in Review* (see Rosen and Foster in Suggested Reading). The differential diagnosis is extensive, but constitutional delay of growth and development accounts for most cases. It

frequently is familial and can be suspected by the characteristic childhood growth curve. Evaluation of bone age can be helpful when constitutional delay is suspected. Because bone age parallels developmental age more closely than chronologic age, it is reassuring when bone age is similarly delayed.

In constitutional delay, once puberty begins, its course is normal, although often at an unusually slow tempo. Final development is not affected. A pathologic cause of pubertal delay should be suspected in the presence of congenital anomalies, concomitant short stature, concomitant endocrinopathies, or when girls have either galactorrhea or signs of virilization. Frank growth arrest after previously normal growth also demands further evaluation.

Summary

Adolescence is a complex process that involves psychological and social maturation alongside the physical growth and development of puberty. Puberty itself is characterized by diversity and variation, although the progression through puberty is remarkably consistent. Ongoing monitoring of growth and development during adolescence helps to identify potential pubertal problems, most of which eventually are proven to be constitutional delay. Regular medical visits during adolescence also provide clinicians with the opportunity to offer preventive guidance to adolescents and their families during an exciting but challenging period of change.

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PIR Quiz

Quiz also available online at www.pedsinreview.org.

6. There are gender differences in the age at which the growth spurt occurs. Among the following, the pair that *best* describes the Sexual Maturity Rating (SMR) stage at which the growth spurt occurs in boys and girls is:

	Boys	Girls
A.	Genital 2	Breast 2
B.	Genital 2	Breast 3
C.	Genital 3	Breast 3
D.	Genital 4	Breast 3
E.	Genital 4	Breast 4

7. An adolescent male in your practice complains of gynecomastia. At what SMR stage of genital development do up to 50% of boys develop noticeable breast tissue?

- A. 1.
- B. 1 to 2.
- C. 2 to 3.
- D. 3 to 4.
- E. 5.

8. You suspect constitutional short stature in a 14-year-old boy who is 5 ft 3 in (160 cm) tall. Among the following, the clinical finding that is *most* supportive of this diagnosis is:

- A. Bone age of 12 years.
- B. Diagnosis of cystic fibrosis.
- C. Elevated alkaline phosphatase activity.
- D. Genital SMR of 4.
- E. Low thyroid-stimulating hormone level.

9. Among the following, the clinical sign *most* associated with the onset of puberty in boys is:

- A. Deepening of the voice.
- B. Elongation of the scrotum and thinning of scrotal skin.
- C. Facial hair.
- D. Penile enlargement.
- E. Sperm in seminal fluid.

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